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Special articles in this issue

THERAPEUTIC ABORTION FROM STANDPOINT OF NEUROPSYCHIATRIST
Franklin G. Ebaugh, M.D., PROFESSOR OF PSYCHIATRY, AND
Keith D. Heuser, M.D., UNIVERSITY OF COLORADO SCHOOL OF MEDICINE, DENVER

ACUTE AND CHRONIC PANCREATITIS
Moses Behrend, M.D., SERVICES OF THE JEWISH AND MOUNT SINAI HOSPITALS, PHILADELPHIA

BACTERIOLOGIC AND SEROLOGIC STUDIES IN EPILEPSY AND SCHIZOPHRENIA I.
Edward C. Rosenow, M.D., BACTERIOLOGIC RESEARCH LABORATORY, LONGVIEW HOSPITAL, CINCINNATI

RELATION OF THE EMOTIONS TO PHYSICAL DISCOMFORT
James E. Paullin, M.D., PROFESSOR OF CLINICAL MEDICINE, EMORY UNIVERSITY, ATLANTA

ENTEROGASTRONE IN MANAGEMENT OF PEPTIC ULCER
H. Marvin Pollard, M.D., ASSOCIATE PROFESSOR OF INTERNAL MEDICINE, AND
Malcolm Block, M.D., UNIVERSITY HOSPITAL, UNIVERSITY OF MICHIGAN, ANN ARBOR

Scientific Exhibit
TECHNIC OF OPERATION FOR FREE COMPOSITE GRAFTS OF THE NIPPLES IN MAMMARYPLASTY
William M. Adams, M.D., MEMPHIS

COMPLETE TABLE OF CONTENTS ON PAGE 5

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Psychiatric Aspects of Therapeutic Abortion

FRANKLIN G. EBAUGH AND KEITH D. HEUSER

UNIVERSITY OF COLORADO SCHOOL OF MEDICINE AND HOSPITALS, DENVER

THE problem of therapeutic abortion has never been entirely resolved to the satisfaction of many physicians. Social, moral, theological, economic, ethical, and legal factors combined with professional judgment frequently make the problem of interruption of pregnancy a complex one. It is felt that no doubt many physicians who have an open mind on the subject are reluctant to discuss it openly not only because they fear the criticism of their colleagues but because they have the more or less unconscious feeling that if one dwells too heavily on the topic, it may give the impression that one is carrying on some shady uterine manipulations.

RELIGIOUS ASPECTS

The religious aspects of abortion are manifold. Because pregnancy is so closely associated with the origin of human life and religious dogmas, theological resistances to therapeutic abortion of any type are encountered constantly. Early Greeks and Romans condoned abortion when necessary. In the Jewish Talmud there are many admonitions against abortion.

For centuries the Christian church has taken the point of view that pregnancy should not be interfered with. Modern-day Protestants, however, in general agree that a therapeutic abortion is acceptable in order to save the life of the mother. On the other hand, the Catholic church has remained inflexible and obdurate against abortion at any time or for any purpose. Perhaps the moral conduct of the individual in society is the basic reason religious leaders feel so opposed to medical intervention with the works of God.

LEGAL ASPECTS

In some localities in America physicians accomplishing a therapeutic abortion might do well to consult the local statutes, since laws have notoriously lagged behind medical science and progress. Harris[9] has made an excellent study of abortion laws. In the vast majority of cases the law exempts from prosecution any person who procures an abortion for the purpose of saving the mother's life whether that person is a physician or not. In some instances the law indicates the advisability of medical consultation in deciding about an abortion. Since there are far more cases in which the future health of the mother, rather than her

FRANKLIN G. EBAUGH

life, are affected by pregnancy, four states make provisions for such a situation—Colorado, the District of Columbia, Maryland, and New Mexico.

It is well known that every possible means of escape is employed by the attorney for a professional abortionist, and not infrequently the jury finds the abortionist not guilty despite a mass of incriminating evidence. The more experienced criminal abortionist makes certain that neither the mother nor any of the family ever see him. Unless murder is involved, it is a fairly safe bet that the abortionist standing trial will be acquitted in the majority of cases. Very inaccurate and few figures are available regarding the convictions for criminal abortions in the United States. Rongy[14] shows that, according to the New York County Medical Society, only three abortionists were convicted and sentenced during a ten-year period, and all three were later pardoned by the governor. In many cases, the abortionist who is convicted is not a duly licensed physician but an impostor, a naturopath, a chiropractor, or a charlatan.

STATISTICS

Certainly in the field of abortion, figures are more than naive. An estimate of the situation has been given by Taussig,[16] who believes that about 700,000 abortions occur annually. The number of abortion deaths is only partly available from the Bureau of the Census, and it has been estimated that at least 10,000 young women lose their lives annually as a result of uterine intervention. In Williams' *Textbook of Obstetrics* the ratio of abortions to confinements is given as one abortion to four or five confinements.

Bearle[2] made an analysis of abortion deaths in the District of Columbia for the years 1938, 1939, and 1940. She found 54 women died of abortions during that period. In connection with 4 of these deaths, 1 abortionist was tried and found guilty, 3 others were exonerated. During this period 12 abortionists were brought before the grand jury of the District of Columbia and 7 were indicted, including 2 licensed physicians, 1 forger, 1 auto mechanic, and 1 post-office clerk.

ENDOCRINE RELATIONSHIPS

The interrelationships between the endocrine system and emotional tensions and conflicts are intimate, complex, and of the greatest psychosomatic significance. Benedek and Rubenstein[3] have illustrated that the psychosomatic structure of the mature human female is a complex one and that a diversity of emotional reactions can be correlated with specific variations of hormone production.

THE basic normal pattern of physiologic and personality relationships may be stated about as follows: Following menstruation there is a gradual increase for 10 days to 2 weeks of the estrogenic or follicular hormones, and, paralleling this in a psychologic manner, there

is an extratensive feeling with interest in the opposite sex. After ovulation occurs, the effects of the estrogenic hormones are masked by the increase of the corpus luteum hormone, progesterone. Psychologically, with an increase of progesterone, flightiness, irritability, decrease in amount of interest in the opposite sex, and an increased interest in the woman herself occurs. There is an emotional preparation for nidation and motherhood. During the late premenstrual period the ego becomes weak. The emotional state at this time may be often characterized clinically as a depression. Women may be somewhat retarded, sad, apathetic, indifferent, and fatigued, and may show more marked emotional instability. Psychosomatic reverberations sometimes occur during the premenstrual phase, such as migraine, gastric distress, constipation, and skin eruptions. The ultimate goal of the sexual cycle in women is, of course, conception, pregnancy, and motherhood. The pregnant woman is prepared both physiologically and emotionally for her motherhood and for her offspring.

KEITH D. HEUSER

If economic and sociologic pressures from outside sources or bodily and mental disease of some nature result in the completion of a therapeutic abortion and an emptying of the uterus, then the hormonal levels, physiologic processes, and emotions are again reduced to the nonpregnant state. Psychosomatic processes must then return to a correlation with previous nonpregnant hormonal levels. These changes, coupled with ideas of guilt, self-depreciation, some recurrent preoccupation centering around infanticide, and the general theme of "I let them kill my baby," might well disturb a poorly integrated personality even to psychotic proportions.

Feelings of love, admiration, and respect for the male partner as a result of pregnancy may well be distorted in the aborted woman to ruminations of disgust, hate, and disrespect: "He gave me a baby and then took it away." The unconscious motivation and the ebb and flow of emotions during the readjustment to a "normal" sexual nonpregnant cycle may result in deeply ingrained feelings of hostility toward the husband. Thus the desire for heterosexual experience may be stifled.

The psychic apparatus, it has been shown, reacts strongly to inadequate estrogen production, and the abrupt change to the nonpregnant status is usually manifested by many of the psychosomatic reverberations listed by Hamilton.[7] Abortions leave a psychologic cicatrix.

In a follow-up study by Hamilton of the psychologic attitude of 100 patients following abortion, the following symptoms were found, the presence of which before abortion was denied: weakness, tiredness, abdominal pain, leukorrhea, depression, backache, constipation, abnormal bleeding, urinary dysfunction, headache, nervousness, fainting. Changes occurred in the patients' attitude toward the abortion, toward their sexual partners, and toward coitus. A general tendency toward depression was demonstrated. Forty-three per cent had not resumed sexual relations as yet. Of 70 patients who at the time of the abortion had expressed love for their partner, 15 had changed to mixed

emotions or dislike. In 13 cases the sex relationship which had been responsible for the pregnancy had terminated with feelings of dislike on the part of the woman. Of 68 women who had stated in the hospital at the time of the abortion that they found pleasure in coitus, 22 expressed indifference and 10 expressed dislike after return to the home environment.

Low hormone levels and psychologic changes as the result of a therapeutic abortion may be characterized in behavior ranging from a regression of the sexual urge to less well-organized tendencies such as depression, withdrawal from social contacts, self-destructive ideas, hostility toward masculine objects, or a recurrent desire to become pregnant.

Hormones influence sexual and the maternal interest and, conversely, the hormonal level may be affected by the emotional state. It is common knowledge that emotional disturbance can suppress menstruation.

Grossesse Nerveuse is a case where a woman firmly believes herself to be pregnant and develops objective symptoms of pregnancy in the absence of it. The dramatic way in which all the symptoms subside when the patient is informed she is not pregnant is amazing.

Spontaneous abortion may occur following emotional shock. In attempting to explain the actual mechanism, the possibility of hyperemia of the uterine vessels must be considered. The increased blood flow to the uterus could lead to hemorrhage into the decidua or cause a premature separation of the placenta.

FRIGIDITY AND STERILITY

It has been previously pointed out that not infrequently an abortion may leave the woman with ambivalent or openly hostile feelings directed toward her marital partner. This disinterest in coitus may vary from failure to obtain an orgasm to a general aversion to coitus. There exists a fairly widespread belief among women that conception is possible only after a complete orgasm. Many women remain in a frigid or semi-frigid state during coitus and, as the result of psychologic and emotional blocking fail to allow their physiologic desire to be expressed. The cause of this blocking in many instances is purely an economic one. "Babies cost too much—think of college and everything." It is true that fear of criticism or ridicule, hostility against the partner, or conflicting love objects are also frequent etiologic factors causing frigidity. The fear of pregnancy stemming from economic distress and financial concern evidencing itself in some type of frigidity must, however, not be underestimated.

One of the sequelae of frigidity may be sterility. A psychogenic resistance to pregnancy can certainly influence the course of conception or pregnancy in an unfortunate way, probably by influencing muscular, circulatory, hormonal, and metabolic processes.

Orr[13] believes that in cases in which women have become pregnant after years of sterility, the emotional change following the adoption or the decision to adopt a child makes psychogenic sterility a probable clinical entity. The influence of psychic factors on hormonal and endocrinologic processes further substantiates such a possibility. Whether the musculature of the uterus is subject to psychic influences or not is still open to debate. Premature labor not infrequently may occur after a sudden fright, so it is assumed that the uterine musculature may possess some reflex activity resulting from emotional excitability.

INDICATIONS FOR THERAPEUTIC ABORTION

It is not within the scope of this paper to discuss in detail the many indications for the performance of a therapeutic abortion. Kuder and Finn[10] have made a report based upon the experience of the New York Lying-in Hospital, from September 1932 through December 1943, with 280 pregnancies which were interrupted for therapeutic reasons. Toxemia and cardiac disease accounted for 58.2 per cent of all the interruptions. Pulmonary and urologic disease accounted for 20.7 per cent and neurologic and psychiatric disease, 5.7 per cent. Of pregnancies

interrupted for neurologic and psychiatric reasons, the majority were for manic depressive psychoses; 3 were for epilepsy along with extenuating circumstances, and 3 for far-advanced cases of multiple sclerosis.

The authors reviewed 29 cases of therapeutic abortions performed at the Colorado General and Colorado Psychopathic Hospital between January 1937 and January 1946, and the results are set forth in Table 1.

TABLE 1

Group	Number of Cases	Per Cent
Toxemia	6	20.7
Cardiac disease	5	17.5
Pulmonary disease	4	13.8
Urologic disease	3	10.3
Neurologic and psychiatric disease	5	17.5
Medical disease	2	6.8
Endometritis	2	6.8
Carcinoma of the cervix	1	3.4
Deformed fractured pelvis	1	3.4
Total	29	100.0

A therapeutic abortion was performed on the following cases of neurologic and psychiatric disease: (1) grand mal epilepsy with psychopathic personality; (2) obsessive, compulsive ruminative state superimposed upon psychopathic personality coupled with pernicious vomiting of pregnancy; (3) mental retardation with choreo-athetosis; (4) Friedreich's ataxia; and (5) recurrent schizophrenia.

In 1937 the University of Colorado School of Medicine and Hospitals formed an Abortion Committee to handle the discussion and decision of cases presented for consideration for a therapeutic abortion. This committee consists of a professor of medicine, a professor of obstetrics and gynecology, and also a professor of psychiatry.

Each consultant gives his decision on the cases and signs his written opinion. This spread of authority prevents any physician from abusing the procedure or utilizing it for selfish gain; it also protects the individual physician since there is a group opinion.

In considering the indications for therapeutic abortion in neurologic and psychiatric disease, one is at the outset confronted with the complex problem of heredity, genetics, and constitutional factors. Genetic aspects of personality are complex because a personality is a somewhat intangible entity and is not subject to rigid types of yardstick measurement. The age-old controversy of heredity versus environment will not be re-hashed here; however, abnormal personalities with social aberration have been studied from social and economic aspects. Sometimes the degree of social problem presented is most marked in the economic sphere. There is a tendency for low economic status to affect numerous members of the same family.

Morally, it would be gross stupidity in the minds of some for the medical profession to condone therapeutic abortion for economic or sociologic reasons, yet one cannot help but wonder what effect such a policy might be in terms of juvenile delinquency, alcoholism, mental deficiency, suicides, homicides, arrests, and the population of our penal and state institutions. The chief objections to therapeutic abortion for economic reasons would be moral, sociologic and, of course, religious.

The decline of the birth rate is rarely disputed by anyone. The decline is probably more pronounced in the well-to-do families than in poor families. Some eugenists feel that the superior are not propagating themselves and the inferior are.

Deutsch[5] feels that every woman has the right to achieve or renounce motherhood and that every woman assumes this right emotionally, whether it is legal or not. The increasing entrance of women into social and economic activity has characterized the American economy for several decades. As the feeling of the individualiy of the woman and her independence increase, her aversion to uncontrolled child-bearing increases.

In a study of 537 cases of abortion at the Bellevue Clinic Hamilton[8] found that the single, the white, the employed, the native American, and the more highly educated woman was found more frequently in the group who

admitted induced abortion than among those who denied it.

The importance of legitimate and illegitimate pregnancy has played a major role in society. The offspring born out of wedlock has been branded a bastard, a term of cosmic rebuke. This term reflects the vindictive attitude of society in general that the offspring should be shunned and the mother condemned in order to pay for her illicit and secret erotic play. Left to herself, many an unmarried pregnant woman would probably not consider having an abortion inasmuch as the unconscious desire to bear the child and the maternal instinct itself are greater than the feelings of society. Other single masochistic women may utilize an abortion to punish themselves or they may carry a deep-seated, masculine-directed hostility for years.

In discussing the indications for therapeutic abortion in psychiatry, the ever-present concept of constitutional endowment must be mentioned. In the development of a personality, the amount and quality of constitutional endowment must be considered and certainly should be emphasized in any case considered for interruption of pregnancy.

Medicine has added to constitutional thinking that the physiologic organism must be considered as an integrated unit which reacts as a whole and not in parts. The psychobiologic school of thought has done much to disseminate this idea through medical circles. Among the psychoanalysts, Franz Alexander of Chicago[1] has emphasized that for any analytical procedure to be successful it must deal with the total personality. Research along psychosomatic lines as performed by Dunbar[6] re-emphasizes the need to include the total over-all personality.

Myerson[12] made a comprehensive study on the inheritance of mental diseases. The transmission of mental disease or the inhertitance of insanity is still somewhat ill-defined and a subject of discussion and debate. Strecker and Ebaugh[15] point out that heredity has been overemphasized in evaluating mental disease. It has been shown that mental illness is only slightly higher in families with positive psychiatric histories than that of the general population as a whole.

Lennox[11] has stated that the underlying condition of epilepsy is heritable and has found a similarity in wave patterns of electroencephalograms of members of the same family; however, less than one-fifth of patients have family histories of epilepsy. With the advent of dilantin, tridione, and the massive amount of research now being carried on with anticonvulsant drugs, the consideration of therapeutic abortion in idiopathic epilepsy hardly seems quite feasible.

Huntington's chorea is definitely known to be due to a degenerative process in the brain and is inherited as a Mendelian dominant character. It may be considered as an indication for therapeutic abortion.

There are apparently still some who dispute the etiologic significance of heredity in mental deficiency; however, it is usually considered a mental disease in which abortion may be genogenically indicated.

ONE of the clinical "wastebaskets" of psychiatric nosology and therapy is the psychopathic personality. Some authors feel that the psychopath is an individual inadequately equipped from birth; however, an etiology of constitutional deficiency remains to be proven. A psychopath externalizes his aggression and works it out on the environment. Usually at an early age, abnormal emotional reactions have occurred which have cemented his early dislike of the world in general. Psychopathy appears to become more and more a socio-characterlogical disease rather than a constitutional one. At the present time there is no indication for performing therapeutic abortion in psychopathy per se. Toxic psychoses due to alcohol, drugs, or other exogenous toxins are rarely, if ever, an indication for therapeutic abortion unless the pregnancy threatens the life of the mother.

There exist very few, if any, psychiatrists who are so partial to their work that they would feel a therapeutic abortion is indicated in any

of the psychoneurotic reaction types. In a certain few selected cases of recurrent schizophrenia in which the illness is of short duration and mild depth, therapeutic abortion may at times be indicated in order to soften the environmental stress as much as possible.

The mode of inheritance in the manic-depressive psychoses is still undetermined, but it would appear to be more hereditarily determined than the other major reaction types. Again, then in certain chosen and selected cases of manic-depressive psychoses, the interruption of pregnancy may be advisable owing to the inability of the patient to care for the child and the problems inherent in management, confinement, and labor. In pregnancy occurring in the single young woman with resultant self-guilt and self-depreciation, coupled with strong energetic suicidal drives, the interruption of pregnancy should be carefully considered and each case, of course, based on its own merits. Buchler[4] feels that it is beyond dispute that spinal and cerebral tumors, syringomyelia, progressive spinal muscular atrophies, hereditary chorea, lateral sclerosis, and severe forms of epidemic encephalitis form absolute indications for abortion.

SEXUAL EDUCATION

Psychiatric reflections on the problem of abortion must, of course, include to some degree the problem of sexual education. Many of our present-day feelings regarding sexual matters are still throwbacks to grandmother and her puritanical turned-up nose; whenever sex reared its ugly head, it was pushed off into the corner to lie hidden, cloaked in all its mystery and darkness. Is it possible that our present-day thinking regarding abortion is still pedantic and locked up in logic-tight compartments?

The family pattern and the parent-child relationships are the nuclei on which personality structure is based. It is our challenge and our duty as physicians in one, if not the most important, branch of public health and preventive medicine, to see that proper parental attitudes and child-parent relationships are established. Daily one meets unbelievable ignorance and naiveté with regard to sexual matters that have produced warped personalities and distorted philosophies of life.

It is easy for the parent to push the responsibility for proper sexual education to the school system, but too frequently the schools are not prepared to accept the responsibility, and, still too frequently, maladjusted teachers feel that sex is a dirty and nasty topic and will have nothing to do with it. Is it not odd that in our present-day school curriculum up to and including high school, courses designed to aid one in meeting the emotional problems of living are not included? World War II with its psychiatric rejection rates and neuropsychiatric casualty lists certainly points to, among other things, a drastic revision in our educational system of today.

The importance of an hour or two spent in premarital counseling may save years of emotional distortion. A few minutes' explanation to the adolescent girl on the eve of her menarche, or to the adolescent boy on the subject of nocturnal emissions may change the pattern of their future adjustment. It is well-known that the parents' personalities, their capacity for love, their acceptance or rejection of sexuality, influence the children's identification and their subsequent psychosexual adjustment. Proper education regarding birth control is, of course, fundamental. Some young married couples start their lives together with a very firm feeling that to have offspring is to admit openly to the world that they are unable to curb their basic instinctive urges and are hanging economic millstones around their necks that will interfere with their own narcissistic gratification of life for years to come.

Childhood is the formative period of life during which the person should learn how to organize all his basic and instinctive urges in a way satisfactory to himself and society. If the child receives little, if any, training regarding sex from his parents or if he receives faulty information from outside sources, then the sexual

expression carried forth into adult life may be distorted and bizarre. If parental attitudes are faulty, they result in serious interference with the usual normal course of psychosexual development.

Adequate and proper sexual education by parents and a well-balanced comprehensive curriculum of sex education in the public school system will go a long way toward establishing a proper outlook on life, maturity, and marriage with its problems and gratifications.

The medical profession must face the abortion problem with realism and a positive attitude as to the complexity of the factors involved.

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Courtesy, Norlyst Art Gallery

ANESTHESIA, by Leonard Lionni. Born in Amsterdam, in 1910, Lionni lived successively in Holland, Belgium, France, Switzerland and Italy. He graduated from the University of Genoa with a Ph. D. in Economics, but art soon became his principal interest. In 1939 Lionni moved to the United States and became a citizen of this country. He now lives in Philadelphia.

Use of Enterogastrone in Management of Peptic Ulcer

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ENTEROGASTRONE is a humoral agent derived from the intestinal mucosa. Up to the present time it has not been obtained in pure crystalline form, but it can be identified by its primary physiologic action of inhibiting the motor and secretory activity of the stomach. The possibility of the existence of such a gastric inhibitory substance has been suspected for a great many years. As long ago as 1886 Ewald and Boas[1] demonstrated that the ingestion of neutral fat inhibits gastric secretion. It was later proven that this effect is elicited from the small intestine and not the stomach.[2] More recently it has been shown[3] that the ingestion of fat inhibits not only gastric secretory activity, but also gastric motility, and that this inhibition of motility is humoral in nature. The concept of the humoral mechanism of this inhibition is a comparatively new one, but it has been adequately proven by the demonstration that the motility of autotransplanted gastric pouches (completely denervated) is inhibited by the introduction of fat into the main stomach. That fact that the inhibition of gastric secretion following the ingestion of fat is also humoral in nature has been proven by the same method.

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The next step in the development of enterogastrone was to find the humoral agent. The first clue to its identification was provided by the observation that cholecystokinin administered in large quantities inhibited gastric secretion.[5] Cholecystokinin is a humoral agent that activates the gallbladder, and since it is prepared from an extract of the small intestine, several extracts were prepared from the mucosa of the small and large intestines of dogs,[6] and it was found that such extracts free of cholecystokinin activity inhibited both the secretory and the motor activity of the stomach. Because of the derivation of this material from the intestine it was named enterogastrone. Later the extract was purified and made more potent, and a "dog unit" was defined on the basis of the degree of inhibition of gastric secretion in dogs.[7]

In view of the long-known relationship between gastric acidity and peptic ulcer in man, the therapeutic possibilities of enterogastrone were early recognized. However, prior to attempting its use in man it was necessary to demonstrate the effect of this substance in experimental ulcers in animals. One form of the experimental approach to human peptic ulcer is the jejunal ulcer that can be produced in dogs by permitting the acid gastric juice to

H. MARVIN POLLARD

come directly and continuously into contact with the sensitive mucosa of the jejunum. This has been accomplished by an anastomotic operation proposed by Mann and Williamson,[8] and animals so prepared are known as Mann-Williamson dogs. In such animals a jejunal ulcer will develop in more than 98 per cent of the cases.[9] It was first demonstrated by Hands and others[10] that when enterogastrone is administered parenterally to Mann-Williamson dogs, jejunal ulcers do not develop. It was shown not only that enterogastrone prevented the formation of jejunal ulcers during the period of therapy with enterogastrone, but also that the use of this substance provides some degree of "immunity" against the development of ulcer. Animals so treated failed to develop a jejunal ulcer long after therapy was discontinued.[11] The mechanism of this protective action is unknown.

In applying these facts to the therapeutic use of enterogastrone in human peptic ulcer, several points must be kept in mind. First of all, there is no certainty that the Mann-Williamson ulcer in dogs can be justifiably identified with the spontaneous gastric or duodenal ulcer in man. Perhaps it is more closely allied to the marginal jejunal ulcer that occasionally follows anastomotic gastric surgery. Recent and interesting data relevant to this problem are provided by the fact that gastric and duodenal ulcers have been unintentionally produced in patients during desensitization with histamine.[12, 13] In all respects these resembled the spontaneous human peptic ulcer. On the other hand, enterogastrone fails to prevent histamine ulcer in dogs.[14] Thus, we have a type of ulcer —quite analogous to spontaneous ulcer—that has been produced in man, but against which enterogastrone provides no protection. A second factor is that enterogastrone can be prepared only as impure extract so that one is unable to be certain that its activity is due to a single substance or to a mixture of two or more substances. In the third place, a very important consideration in determining the value of enterogastrone in treating peptic ulcer is the fact that both the gastric and duodenal ulcers during their natural history undergo spontaneous remissions and exacerbations. This accounts for the many forms of therapy that have been advocated and provides an important stumbling block in critically evaluating the specific efficacy of any single agent such as enterogastrone.

From a critical point of view, it appears to us that any agent to be considered of *fundamental* therapeutic value in peptic ulcer must fulfill two qualifications: It must shorten the duration of an acute exacerbation, and it must prevent the recurrence of either gastric or duodenal ulcer, at least during the period of its administration.

KEEPING these facts in mind we may now consider the results of enterogastrone therapy in man. The first report of such a clinical trial was reported in 1943[11] and has recently been amplified by Greengard and his co-workers.[15] Fifty-eight patients were treated with in-

tramuscular enterogastrone. Of these, 51 had duodenal ulcers, 4 had postoperative jejunal ulcers, 2 had both a gastric and a duodenal ulcer, and 1 had a gastric ulcer. Twenty-six patients received 6 injections weekly and 32 received 3 injections each week. Treatment was carried out for 6 to 12 months, and the authors reported that a large number of the cases had no recurrences during and after therapy and that there was improvement in the radiographic appearance of the upper gastrointestinal tract. They felt from their results that it was admissible to state that in their 58 cases the parenteral administration of enterogastrone was not without beneficial consequences.

MALCOLM BLOCK

Up to the present time there have not appeared in this country any other reports on the clinical use of *parenteral* enterogastrone or any reports on the clinical use of *oral* enterogastrone. However, for several years results of the use of crude extracts of duodenal mucosa and submucosa by oral administration in peptic ulcer in man have been published, and quite recently several European investigators[16, 17] have reported on the use of such crude extracts both orally and parenterally. These results are difficult to evaluate because in most instances the extracts were neither adequately purified nor standardized. In addition, the extracts employed have varied from investigator to investigator and, in many instances, were mixed with extracts of the gastric mucosa. Of historical interest is the Rivers[18] report giving encouraging results obtained from the oral use of crude duodenal extracts in 50 patients. These reports all raise the problem of the possible use of enterogastrone orally in man for peptic ulcer. Apparently, oral administration of this material protects Mann-Williamson dogs against jejunal ulcers.[9] Likewise, it has been recently demonstrated[19] that large quantities of hog stomach and duodenal preparations protect dogs against cinchophen ulcers. However, there has been no clinical data on the oral use of the purified preparation of enterogastrone in man.

Our own experience with the clinical use of enterogastrone has involved its use in gastric and duodenal ulcer, administered both orally and intramuscularly. It was felt that more information could be obtained from a careful clinical roentgenologic and laboratory study of a comparatively small group of patients followed carefully than from its indiscriminate use in every case of peptic ulcer. Three criteria were established for the selection of patients as suitable for treatment with enterogastrone. First of all, we required a long history of recurrent exacerbations of peptic ulcer. Actually, most of the patients treated had an average of 2 yearly recurrences for a period of at least 5 years. Secondly, patients were selected on the probability of their cooperation for long-continued observation and follow-up. Thirdly, with one exception, we did not undertake enterogastrone therapy in those cases where complications, particularly pyloric obstruction, were present in the patient.

Selected on the basis of these criteria, we have treated up to the present time 31 cases

TABLE 1

FIFTEEN CASES OF PEPTIC ULCER TREATED WITH ORAL ENTEROGASTRONE

Case	Diagnosis*	Duration of Symptoms (Years)	Daily Dosage (Grams)	Duration of Therapy (Months)
1	DC	17	8.0	13
2	D	15	16.0	6
3	D	16	8.0	8
4	D	12	16.0	4
5	D	8	16.0	4
6	D	20	16.0	2½
7	G	11	16.0	8
8	DC	5	16.0	4
9	D	6	16.0	4
10	DC	21	16.0	6
11	DC	10	8.0	9
12	D	10	8.0	11
13	D	6	16.0	4
14	D	8	16.0	1½
15	D	3	16.0	1½

*D, duodenal bulb deformity; DC, duodenal ulcer crater; and G, gastric ulcer.

TABLE 2

SIXTEEN CASES OF PEPTIC ULCER TREATED WITH PARENTERAL ENTEROGASTRONE

Case	Diagnosis*	Duration of Symptoms (Years)	Daily Dosage (Milligrams)	Duration of Therapy (Months)
16	DC	21	200	4
17	D	8	200	6
18	D	17	200	5
19	D	23	200	¾
20	D	15	200	4
21	J	9	200–400	7
22	D	15	200	3½
23	D	10	200	8
24	D	20	16 gm.†	3
			200	4½
25	D	18	200	1½
26	D	9	200	4
27	D	6	200‡	2
			16 gm.	4
28	DG	15	200	4
29	D	12	200	4
30	D	15	200	7
31	D	20	200	3

*D, duodenal bulb deformity; J, jejunal ulcer; G, gastric ulcer; and DC, duodenal ulcer crater.

†Changed from oral to parenteral after three months' therapy at patient's request.

‡Changed to oral because of persistent malaise associated with use of parenteral preparation.

with enterogastrone. The essential data on these cases is presented in *Tables 1 and 2*. It will be seen that 28 cases had duodenal ulcer, 1 had a gastric ulcer, 1 had both duodenal and gastric ulcers, and 1 had a marginal jejunal ulcer subsequent to a partial gastric resection. Fifteen cases were treated by the oral administration of the drug, and 16 were treated by the parenteral route. When given orally, the dosage varied from 8 to 16 gm. daily. At present we usually favor the higher dosage. The intramuscular dose was usually 200 mg. given daily for 6 days of each week. During the initial 3 to 4 weeks of treatment the patient was maintained on a modified Meulengracht diet, antacid medication, and antispasmodics as necessary to control symptoms. Later an effort was made to discontinue all medication except enterogastrone and to broaden the diet to include nearly all foods, except possibly a few items which the patient felt sure elicited symptoms. It was not always possible to accomplish these ends, particularly in regard to diet, because many of our patients had been on restricted diets for so long a time that they actually feared to partake of a general diet. In addition, persistence of symptoms in some cases required a restricted diet and antacid medication.

In no instance was oral enterogastrone responsible for any untoward reactions. On the other hand, intramuscular enterogastrone caused a local reaction characterized by pain and tenderness at the site of injection in every case. This local reaction was often quite severe and usually occurred during the first 10 to 14 injections, but disappeared thereafter and failed to recur. The intramuscular drug also was responsible for systemic reactions in at least 2 instances, and, possibly 4. In 1 case, the systemic reaction occurred in an asthmatic and was characterized by persistent headaches. Concomitant use of pyribenzamine relieved the headache and made it possible to continue the drug. In another instance, general malaise occurred during the parenteral administration of enterogastrone, and only in this case was it necessary to discontinue the injections. In 2 other cases chills and fever were reported as ensuing after the parenteral administration of enterogastrone at the patient's home. This febrile reaction did

not recur subsequently when the patients were observed by us at a later date in the hospital, even though the injections were continued.

We have already pointed out some of the difficulties in evaluating clinical results in the therapy of peptic ulcer. Improper selection of cases may also be a factor such as in Case 19 where organic obstruction was apparently present and in Case 18 where psychogenic situational factors were of paramount importance in producing symptoms. Likewise, it must be remembered that often the patient continued to complain of vague upper gastrointestinal discomfort which was not entirely characteristic of a typical recurrence. However, in such cases one should not conclude that the patient was necessarily an example of successful therapy as far as enterogastrone is concerned. Since treatment has been carried out for periods of three weeks to thirteen months, in many instances our period of observation is not as yet long enough to come to definite conclusions regarding recurrence rate. Considering all these factors, we have attempted to classify the clinical course of our treated cases during and subsequent to enterogastrone therapy. See *Tables 3 and 4* for this classification.

It will be noted that of 16 cases treated orally, 2 subsequently required surgery, 1 had a definite recurrence of his peptic ulcer clinically and radiographically, and 1 had persistent vague upper gastrointestinal symptoms. Twelve cases had a satisfactory course symptomatically. However, 1 case in this last group (Case 7) with a gastric ulcer had persistent symptoms for six months after treatment started. This was the time required for the radiographic healing of the ulcer, and one would be certainly justified in criticizing our inclusion of this case in the successful group. Of the 15 cases treated parenterally, 2 required subsequent surgery, 3 had definite recurrence of clinical symptoms, 2 had persistence of vague upper gastrointestinal symptoms, and in 8 cases the course was entirely satisfactory.

TABLE 3

CLINICAL COURSE OF FIFTEEN CASES OF PEPTIC ULCER TREATED WITH ORAL ENTEROGASTRONE

Required surgery	
Case 4. Persistent symptoms	2
Case 10. Developed obstruction	
Definite clinical recurrence	
Case 12. Clinical and radiographic evidence of exacerbation after ten months	1
Persistent vague symptoms	
Case 11. Vague epigastric distress ? pylorospasm	1
Satisfactory control of ulcer	12

TABLE 4

CLINICAL COURSE OF SIXTEEN CASES OF PEPTIC ULCER TREATED WITH INTRAMUSCULAR ENTEROGASTRONE

Required surgery	
Case 19. Persistence of obstruction initially present	2
Case 22. Developed obstruction	
Definite clinical recurrence	
Case 28. Duodenal deformity at start. Crater appeared after two months' therapy.	3
Case 26. Persistence of symptoms	
Case 31. Persistence of symptoms. Gastric ulcer appeared	
Persistence of vague symptoms	
Case 18. ? pylorospasm	2
Case 27. Pylorospasm	
Satisfactory control of ulcer	8

THE most striking therapeutic result was obtained in Case 21. This patient is a 44-year-old male. He was first seen at the University Hospital in 1938 because he had a severe anemia. At that time a "duodenal ulcer of long standing" was found by x-ray. He was given an antacid and placed on a restricted diet. He was not seen again until December 1946, when he revealed that characteristic ulcer symptoms recurred in September 1940, in association with frequent tarry stools. A partial gastric resection was carried out at another hospital at that time. There were then no symptoms for three years, postoperatively. However, from 1943 to December 1946 there were recurrent symptoms and at least 3 episodes of gastrointestinal bleeding associated with chronic persistent anemia. On

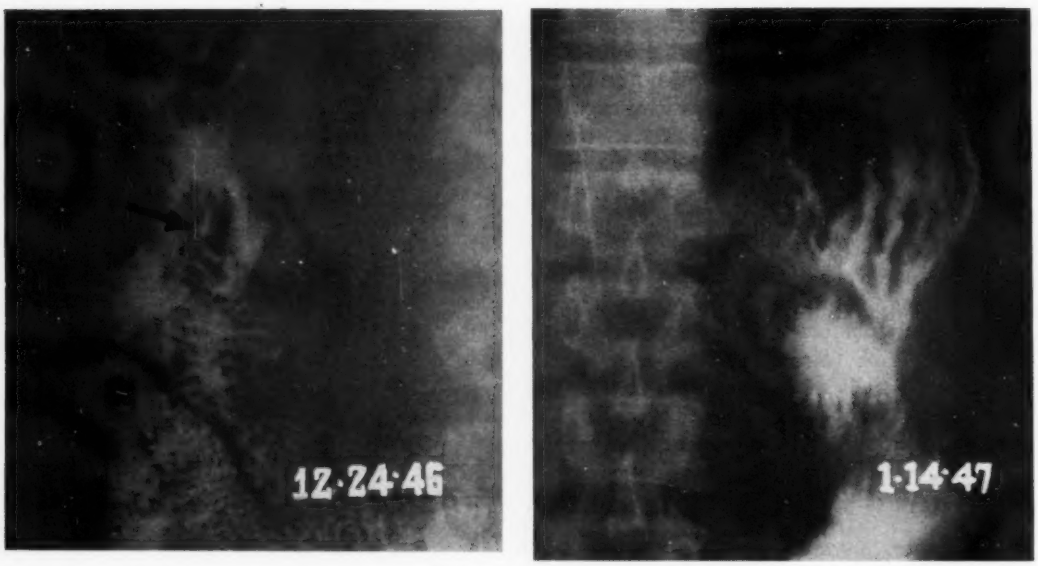

Figure 1. Upper gastrointestinal x-rays in Case 21. Marginal ulcer present 12/24/46. Complete healing by 1/14/47.

December 23, 1946, he was admitted to the University Hospital. At that time the physical examination revealed a pale, undernourished male (weight, 131.5 pounds; height, 68.5 inches). Hemoglobin was 11.1 gm. and the red cell count 5,200,000. Stool was positive for occult blood. A gastrointestinal x-ray made on December 24, 1946, revealed a "marginal ulcer following gastro-jejunostomy" (*Figure 1*). On this date enterogastrone was started, 200 mg. intramuscularly daily. This was increased to twice daily December 30, 1946, and continued until January 28, 1947, when it was decreased to once daily and has been continued at this dosage up to the present. In addition to enterogastrone, the patient was given a bland diet and ferrous sulfate. Repeat x-ray on January 14, 1947, revealed complete healing of the ulcer (*Figure 1*). At this time the patient was asymptomatic, weight was 135 pounds, stools were negative for occult blood, and hemoglobin was 12.0 gm. He was discharged January 29, 1947, and has remained asymptomatic to the present. Hemoglobin is now 14.0 gm. and his weight is 139 pounds at this point.

Another instance of a less striking but definitely successful result associated with enterogastrone therapy is exemplified by Case 1. This patient is a 49-year-old male. He was originally seen at the University Hospital in May 1946, complaining of epigastric discomfort which occurred two to three hours after meals and was relieved by food or alkali. He had had this difficulty since 1929, but had been able to control his symptoms moderately well by restriction of diet, frequent feedings, and the use of sodium bicarbonate. There were many recurrent exacerbations of symptoms, particularly in the fall and winter. During the summer the patient was generally symptom free.

In 1939 an x-ray diagnosis of duodenal ulcer was first made. In December 1944, he had a severe hematemesis requiring hospitalization. Since that time symptoms had been more severe and persistent with occasional recurrent episodes of nausea and vomiting lasting a few days to 2 weeks. When first seen at the University Hospital (May 19, 1946) he appeared well nourished. There was epigastric tenderness. X-rays (May 10, 1946) revealed deformity of

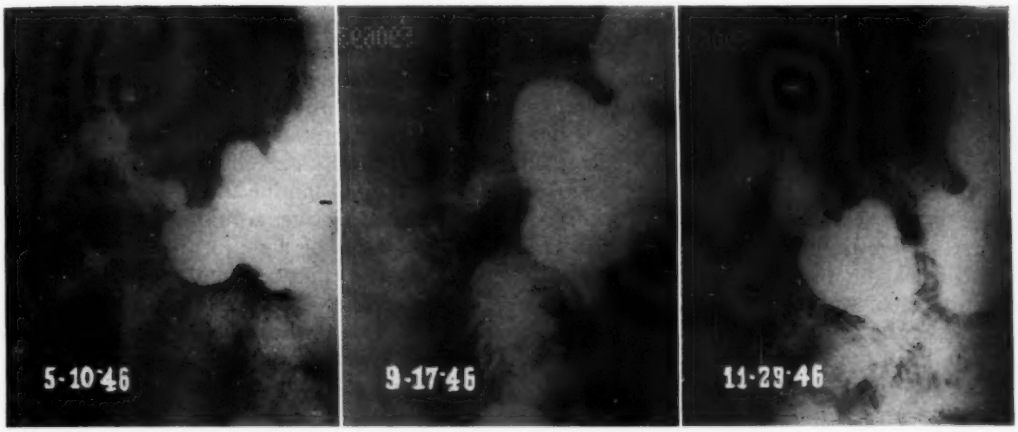

Figure 2. X-rays in Case 1. No marked change from 5/10/46 to 11/29/46 in spite of patient's becoming asymptomatic.

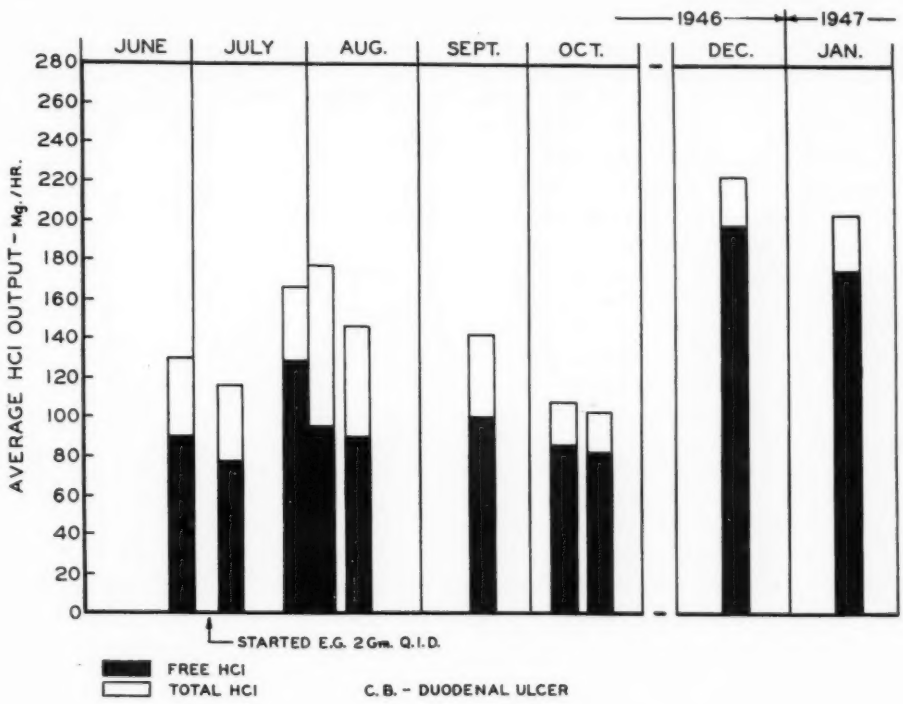

Figure 3. Variations in output of hydrochloric acid during oral therapy with enterogastrone (Case 1).

the duodenal bulb and evidence of a small crater (*Figure 2*). He was placed on a modified Meulengracht diet, and given atropine and oral enterogastrone, 8 gm. daily. Patient became asymptomatic after 2 weeks, when the Meulengracht diet was discontinued. He remained asymptomatic until September 1946, when he had a one-day episode of nausea and vomiting. X-rays at this time (September 17, 1946) revealed marked deformity of the duodenal bulb, but no crater was present (*Figure 2*). Since September the patient has continued essentially asymptomatic. He has gained weight and has lost no time from work. X-rays on November 29, 1946, revealed only duodenal deformity shown in Figure 2.

This case is of considerable interest because of at least two points. First of all, as Figure 2 illustrated, the x-ray appearance of the duodenal deformity is essentially unchanged in spite of nearly complete symptomatic relief. We have found this to be generally true where the diagnosis of peptic ulcer is originally based on the occurrence of the ulcer symptom-complex and the x-ray finding of only duodenal bulb deformity. This is important because in such instances one cannot generally use objective x-ray observation as a criterion of the efficacy of enterogastrone. In cases of gastric ulcer or where a duodenal ulcer crater is present the situation is different. A second point of interest in Case 1 is the absence of any change in gastric secretion and motility in spite of symptomatic relief. As indicated in Figure 3, frequent observations of gastric acidity revealed no change from the period of active symptoms to the time when no symptoms were present. The same thing is true for gastric motility. This has been found to be generally true in our patients, so that whatever effect enterogastrone may have had in relieving symptoms cannot be explained on the basis of the effect of enterogastrone on either the secretory or the motor activity of the stomach.

SUMMARY

1. Enterogastrone is a humoral agent which is derived from the intestinal tract and causes an inhibition of secretory and motor activity of the stomach in experimental animals.

2. Enterogastrone intramuscularly—and possible orally—protects Mann-Williamson dogs against jejunal ulcers, but fails to protect the dogs against histamine ulcers.

3. Enterogastrone administered to patients orally in doses of 8 to 16 gm. daily produces no untoward effects. When given intramuscularly, it nearly uniformly causes a transient local reaction at the site of injection and occasionally a mild generalized systemic reaction.

4. Enterogastrone given either orally or intramuscularly over long periods of time to patients with gastric or duodenal ulcer may have some beneficial effect in decreasing the incidence of exacerbations of the disease.

5. Final conclusions regarding the value of enterogastrone must await (1) further purification of the agent, and (2) the careful observation over a period of years by several different investigators of patients with peptic ulcer treated with enterogastrone.

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Acute and Chronic Pancreatitis

MOSES BEHREND*

PHILADELPHIA

Acute pancreatitis curiously seems to occur in periodic cycles. The real cause of acute pancreatitis is unknown. The precipitating cause, however, is supposed to be an admixture of the pancreatic and biliary juices due to biliary reflux. If this is true, there should be many more cases of acute pancreatitis reported. A hematogenous infection may also cause acute pancreatitis. It is a well-known fact that gourmands and those who drink heavily of alcoholic liquors are especially subject to acute pancreatitis.

Symptoms—Attacks of acute pancreatitis occur with extreme suddenness. There is no acute abdominal pain that can compare with its intensity. The area of the pain is general, usually not localized. The rigidity of the abdomen is boardlike, hard, and nonresistant. The slightest touch causes greater tenderness. This diffuse pain remains for several hours until relief is afforded by large doses of morphine. The fact that large doses of morphine are required to relieve the pain often helps to make a differential diagnosis between a ruptured peptic ulcer and acute pancreatitis.

The serum amylase test is the most valuable method in formulating a diagnosis of acute pancreatitis. In this condition the serum amylase may reach 500 to 3000 units as compared to a normal of 60 to 180 units. Considerable dependence can be placed upon an increase of the serum amylase values in from twelve to twenty-four hours.

Treatment—In the past few years much emphasis has been laid upon delayed operation for acute pancreatitis. There is no question that if a positive diagnosis can be made—and this can be confirmed largely now by the amylase test —a delayed operation is far superior to an emergency operation. The mortality of operating upon acute pancreatitis as an emergency is appalling. Results are excellent if one delays operation for at least a week or ten days. Similar conditions hold in cases of acute cholecystitis where delayed operations are preferable to an emergency type of procedure. There is some resemblance in the resolution of this type of inflammation in these two related organs, namely, the gallbladder and the pancreas.

CHRONIC PANCREATITIS

Disturbances in the right upper quadrant and epigastric regions may be due to chronic pancreatitis. The cause of chronic pancreatitis

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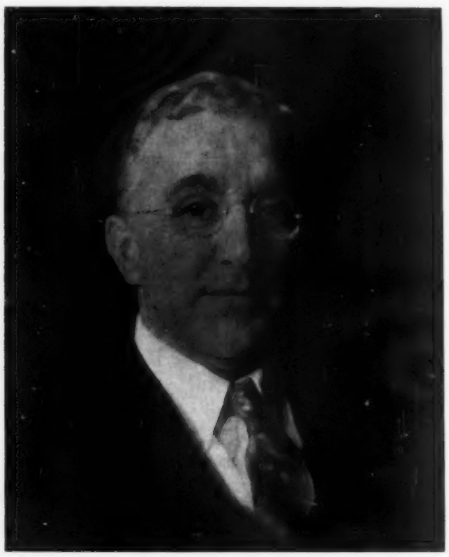

MOSES BEHREND

is not known. Repeated mild attacks of acute pancreatitis may be a factor. In certain cases there may be some relationship between pancreatic fibrosis in infancy and chronic pancreatitis. The majority of cases encountered have no evident causative factor.

Symptoms—The symptoms of chronic pancreatitis vary with the stage of the disease. In mild inflammatory conditions the intensity and exacerbation of pain is less. The pain may simulate exactly that experienced in cholelithiasis. Jaundice may or may not accompany these phenomena. The intensity of jaundice depends also on the state of inflammation of the pancreas. Jaundice usually becomes more intense after the exacerbations of pain. After the attack the jaundice gradually disappears or may remain in a very slight form, with the yellow-tinged conjunctiva being the only evidence of obstruction that remains. In a few cases no jaundice is present at all in those suffering from chronic pancreatitis. Indiscretions in diet may precipitate attacks similar to those found in disease of the bile passageways.

Laboratory tests are of little value. The amylase test so important in acute pancreatitis is of practically no value in the chronic type of infection.

Diagnosis—It is necessary to make a differential diagnosis between chronic pancreatitis, cholelithiasis, and choledocholithiasis. In cases harboring stones in the gallbladder or common duct or both, the x-ray is helpful. A poorly functioning gallbladder with shadows of stones is indicative of gallbladder disease. X-ray of the pancreatic region reveals nothing unless there are calcareous deposits in this area.

Since there are no specific symptoms or laboratory tests, operation must be considered in the final analysis and disposition of the case. Even when the abdomen is open it is not easy to differentiate between chronic pancreatitis and cancer of the pancreas. One must develop a fine sense of touch to recognize by palpation alone the difference between these two conditions. The degree of hardness and the intensity of the jaundice may often be a great help in coming to a conclusion.

When great difficulty is encountered, a biopsy is important. This test was of great importance in a patient in whom there was complete obstruction of the common duct due to chronic pancreatitis. In other cases where obstruction was incomplete, a biopsy also differentiated between chronic pancreatitis and cancer of this organ.

In the course of an operation for gallbladder disease the pancreas should be palpated. This is especially important in patients who do not have cholelithiasis. The removal of the gallbladder where stones are absent only adds more discomfort later. If no stones are found, the gallbladder should be carefully examined for tumors within its walls. Tumors within the gallbladder are not common. They can usually be felt through the walls of the gallbladder. This can be illustrated by a recent case in which an operation was performed; dis-

seminated carcinomatous tumors were found within the gallbladder and one was found in the common duct (*Figure 1*). All the symptoms incident to gallstone colic were experienced by the patient. It was impossible to arrive at a diagnosis because the symptoms were those of cholelithiasis or pancreatitis.

Type of Operation—An external drainage operation of the common duct or gallbladder should never be performed if an internal anastomosis can be made between the hollow viscera and the bile passageways. After a cholecystostomy or a choledochostomy bile will continue to flow externally as long as the patient lives, provided the obstruction continues to persist. Thirty-five years ago surface drainage operations were very popular, but with the refined technic that followed, it became evident that the anastomoses advocated below are far superior to any other type of operation. The anastomosis of the bile passageways with the hollow viscera consists of a cholecystoduodenostomy, cholecystogastrostomy, or cholecystojejunostomy.

When the common duct is used, we may perform a choledochoduodenostomy, choledochogastrostomy, or choledochojejunostomy (*Figure 2*). It has always been my rule to use that portion of the intestinal tract adjacent to the bile passageways. If it is easier to anastomose the stomach to the gallbladder or common duct, that is the structure which is used (*Figures 3 and 4*). Although it is more logical to anastomose the gallbladder and common duct to the duodenum and jejunum, the patient never has any prolonged distress if the stomach is anastomosed to these structures. The danger of infection of the liver which has been of much concern for many years has never deterred me from using the stomach, duodenum or jejunum, because in my experience this occurs very infrequently.

The operation of pancreaticoduodenectomy should be reserved for those cases in which total obstruction is found due to chronic pancreatitis, carcinoma, or calcareous deposits in the pancreas. When a complete benign obstruction exists, the common duct is isolated from its bed, the distal end is ligated, and with the proximal end, an end-to-side anastomosis is performed to the stomach, duodenum, or jejunum (*Figure 5*). These short-circuiting operations have been employed for a decade with benefit to the patient. The history of ten cases has been reported recently.* All recovered except one. He was a man thirty-one years old, with incomplete obstruction of the common duct due to chronic pancreatitis. Three weeks after a choledochoduodenostomy, he died from

Figure 1. Multiple implants of carcinoma of the gallbladder. Diagnosis difficult. Symptoms simulated cholelithiasis or chronic pancreatitis.

*Printed in the Archives of Surgery.

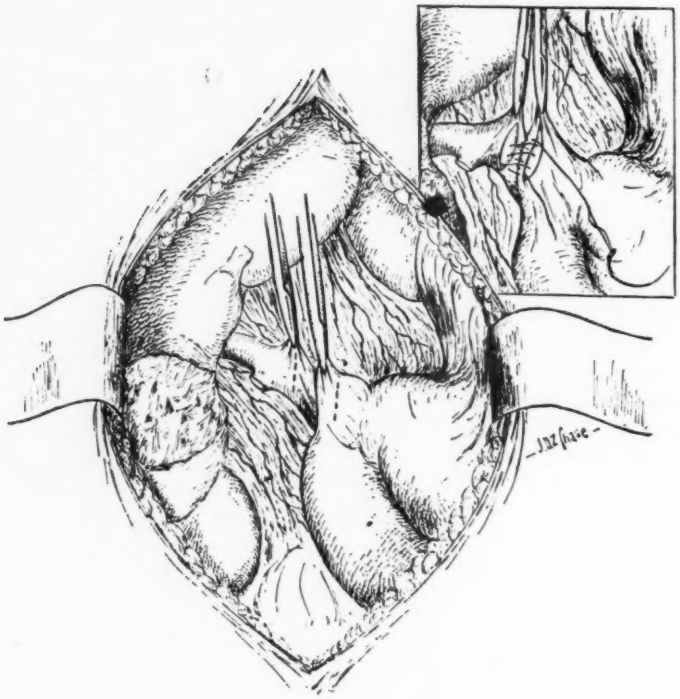

Figure 2. Illustration shows the technic of a lateral choledochogastrostomy. The same method may be used in performing a choledochoduodenostomy.

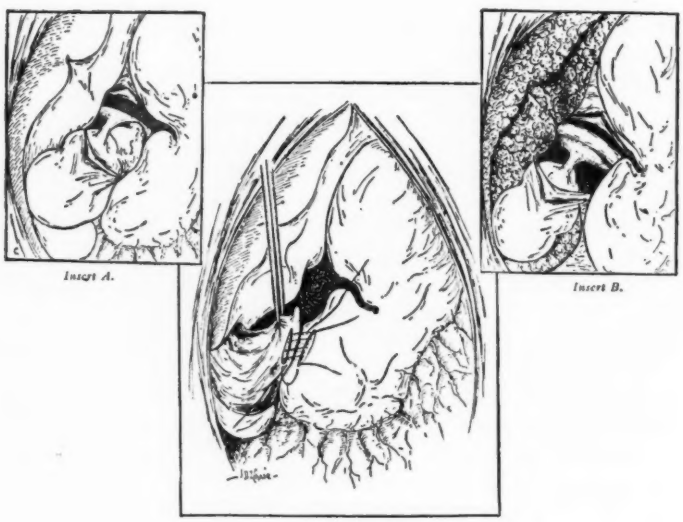

Figure 3. Anastomosis of the stomach to the gallbladder. (Cholecystogastrostomy.)

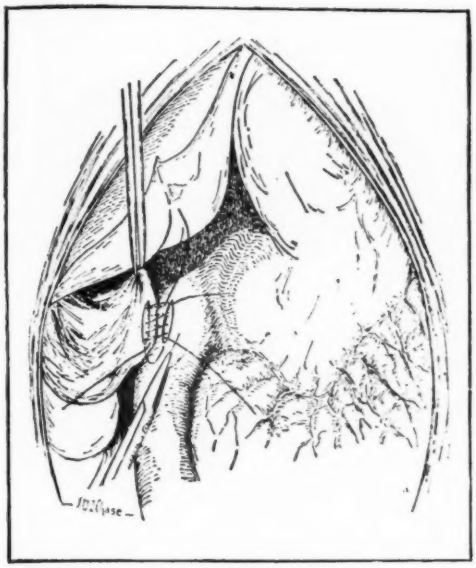

Figure 4. Anastomosis of the gallbladder to the duodenum. The same technic may be used in performing a cholecystojejunostomy.

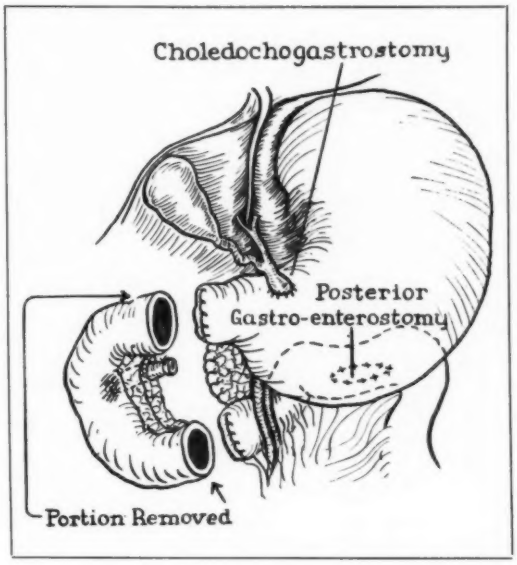

Figure 5. Illustrates an end-to-side anastomosis of the isolated common duct to the stomach. The duodenum or jejunum may also be used.

diabetic acidosis. Another patient in whom a diagnosis of cancer of the pancreas was made died twenty-two years after the performance of a cholecystoduodenostomy; obviously he did not have carcinoma. The remaining eight are living and well.

SUMMARY

The causes of acute and chronic pancreatitis are still unknown. When the diagnosis of acute pancreatitis has been made with the help of the serum amylase test, conservative and delayed surgical attack gives the best ultimate results. Chronic pancreatitis may simulate all the symptoms of cholelithiasis and tumors within the lumen of the gallbladder. Jaundice may be absent, but if present, its intensity is less than that found in cancer of the pancreas. At the time of the operation chronic pancreatitis must be differentiated from cancer of the pancreas. A biopsy is of considerable help. The operations recommended have withstood the test of time for over a decade. They consist of the various anastomoses of the bile passageways with the hollow viscera.

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Bacteriologic, Etiologic, and Serologic Studies in Epilepsy and Schizophrenia I.

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In studies on the etiology of various diseases it was found, in agreement with other investigators, that the aerobic methods usually employed in bacteriology do not suffice for the consistent isolation of causative organisms. By the use of special mediums which afforded a gradient of oxygen tension and other properties favorable for the growth of fastidious organisms, specific types of streptococci which had elective localizing power on injection into animals were isolated consistently in studies of various diseases.[1,2,3,4]

The results obtained in some epidemic[5,6,7,8] and nonepidemic diseases[9,10] have been reported. Those obtained in studies of epilepsy and schizophrenia over a period of a dozen years as opportunity was afforded, although highly suggestive,[11] have been withheld until results of a more intensive study became available. These it is felt are now at hand.

The results of studies on the isolation of alpha streptococci and of experiments in animals in which spasms and convulsive seizures and disorientation and strange symptoms in behavior were produced with the respective strains will be reported elsewhere. Those obtained in agglutination, agglutinin absorption, and precipitation experiments with the antiserums prepared in horses and rabbits and produced in vitro from the respective streptococci and with the serum of persons ill are to be reported in this paper.

This is first of a series of three papers by Dr. Rosenow in which are recorded the results of bacteriologic and experimental studies on the etiology of epilepsy and schizophrenia. Papers II and III will appear in later issues of *Postgraduate Medicine*.

METHODS AND MATERIAL

Realizing the difficulties that have been encountered in the isolation of specific types of alpha streptococci from persons suffering from various diseases and in experiments on agglutination[12] and precipitation, we have used special methods to eliminate these in so far as possible. The diagnoses for the most part were made by examining physicians in charge of patients in hospitals and private practice. Cultures were made from nasopharynx, infected teeth, blood, spinal fluid, urine, and feces.

Nasopharyngeal swabbings were made with swabs wrapped on aluminum wire and bent to a suitable angle without touching the tongue. The nasopharyngeal swabbings and the material obtained from pyorrhea pockets and the severed apexes of pulpless teeth, drawn in a sterile manner, were suspended in 2 ml. of a 0.2 gelatin-Locke or isotonic sodium chloride

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solution for cultures, precipitation tests, and inoculation of animals.

Routinely, the surface of horse blood agar plates were inoculated and serial dilution cultures[13] were made in mediums affording a gradient of oxygen tension, viz. in dextrose brain broth or alternately dextrose brain broth (0.2 per cent dextrose) and soft dextrose brain agar (0.2 per cent dextrose and 0.2 per cent agar) in tall (12 cm.) columns in test tubes. The dextrose brain broth and dextrose brain agar were prepared by adding, before autoclaving, approximately 1 part by volume of pieces of fresh or frozen calf or young beef brain to 6 or 7 volumes of the mediums previously adjusted to *p*H 7.2 and contained in ⅝ x 6- or 8-inch test tubes in columns 12 cm. in height.

THE amount of inoculum in the first tube and degree of serial dilution, usually at steps of 1–100 or 10,000, was determined by the number and kind of organism found in stained films of the material under study. The brain-containing mediums used were freshly prepared or were boiled to drive off dissolved oxygen and cooled to 40°C. immediately before they were inoculated.

Pure cultures for inoculation of animals, and for serologic and other studies were obtained not from blood agar plates but from the end point of growth of usually young primary serial dilution cultures in dextrose brain broth or dextrose brain agar. Blood agar plates were made of these to determine the type of streptococcus and to be sure of the purity of the young cultures.

Pure cultures of streptococci obtained from patients and from animals were routinely preserved in dehydrated form by placing the centrifugated sedimented organisms from young dextrose brain broth or dextrose broth cultures of streptococci after decanting the supernatant broth in very dense suspension (300,000,000,000 per ml.) of glycerol 2 parts and saturated sodium chloride solution 1 part. Moreover, selected strains of streptococci were inoculated into previously warmed 0.2 per cent dextrose broth in gallon bottles containing 3500 ml. each, and the organisms of young cultures from a continuous feed centrifuge bowl were likewise preserved at 10°C. in dehydrated form in dense suspension of the glycerol–sodium chloride solution menstruum (1,000,000,000,000 organisms per ml.) for agglutination and precipitation tests, for immunization of horses and rabbits, and for the preparation of solutions of specific polysaccharide and thermal antibodies.[14]

The agglutination tests were made by placing 0.2 ml. of fivefold dilutions of 1–20 to 1–2500 of the serum or thermal antibodies into test tubes ⅜ x 3 inches and adding to each tube 0.2 ml. of the respective suspensions of streptococci containing approximately 5,000,000,000 organisms per ml. The suspensions were allowed to stand at room temperature or were lightly centrifuged to eliminate clumped organisms. The setups were thoroughly shaken and placed in the incubator at 47°C. to 50°C. for eighteen to twenty-four hours.[12] Readings were made in a dark room under the edge of a shaded light

TABLE 1

ILLUSTRATIVE EXPERIMENT ON THE AGGLUTINATION OF STREPTOCOCCI BY THE SERUM OF PATIENTS

Source of Streptococcal Pools	Dilutions of Serums and Per Cent of Agglutination	Degree (0-4) and Percentage of Total Possible Agglutination at Fivefold Dilutions of Pools of 5 Serums Each of Well Persons and of Persons Suffering from:			
		Epilepsy	Schizophrenia	Arthritis	Control well persons
Epilepsy (11)*	1-20	**2**	3	2	2
	1-100	**2**	3	2	2
	1-500	**3**	0	0	0
	1-2500	**3**	0	0	0
	Per cent	**63**	38	25	25
Schizophrenia (10)	1-20	3	**3**	2	2
	1-100	3	**3**	2	2
	1-500	2	**3**	0	0
	1-2500	0	**2**	0	0
	Per cent	50	**69**	25	25
Arthritis (30)	1-20	2	2	**2**	2
	1-100	2	2	**3**	2
	1-500	2	0	**3**	0
	1-2500	0	0	**3**	0
	Per cent	38	25	**69**	25
Control pneumococci (9)	1-20	2	2	2	2
	1-100	0	2	0	0
	1-500	0	0	0	0
	1-2500	0	0	0	0
	Per cent	13	25	13	13

*The figures in parentheses indicate the number of strains in pools.

from a 100-watt electric light bulb against a nonreflecting background of black velvet cloth. The degree of agglutination was recorded without regard to the source or type of antibody according to the arbitrary scale of 0 to 4 plus.

Two types of thermal antibodies were used in agglutination and precipitation tests. The one designated simply as thermal antibody represented the bacteria-free supernatant of suspensions in sodium chloride solution containing 10,000,000,000 streptococci per ml. after autoclaving at 15 to 17 pounds pressure for ninety-six hours.[14] The other designated as thermal hydrogen peroxide antibody represented the bacteria-free supernatant of suspensions in sodium chloride solution containing 10,000,000,000 streptococci per ml. which were autoclaved for one hour after adding 1.5 per cent H_2O_2 (initial).[15] The respective streptococci in both instances represented dilutions of the partially dehydrated organisms from dense suspensions in a mixture of glycerol and saturated sodium chloride solution.

Agglutinin absorption experiments were done by adding approximately 5,000,000,000 of the washed organisms per ml. from the dense suspensions in glycerol–sodium chloride solution to the respective undiluted serums and thermal hydrogen peroxide antibody. The first two absorptions were done by incubating for one and one-half hours at 35°C. and the third absorption at 35°C. for one and one-half hours and at 10°C. for eighteen hours. The respective suspensions were centrifuged, the serum or antibody was decanted, and the agglutinin titer of the absorbed and unabsorbed serums determined in parallel manner.

For the sake of brevity and in order that the degree of agglutination of the different strains by the four dilutions of the different materials

TABLE 2

AGGLUTINATION OF ALPHA STREPTOCOCCI ISOLATED FROM THE NASOPHARYNX OR BLOOD OF PERSONS SUFFERING FROM EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY THE ANTISERUMS* PREPARED IN HORSES WITH THE RESPECTIVE STRAINS OF STREPTOCOCCI.

Source of Streptococci	Streptococcal		Agglutination Experiments	Percentage of Total Possible Agglutination at Fivefold Dilutions of 1-20 to 1-2,500 of Antiserums Prepared in Horses with Streptococci Isolated in Studies of:		
	Pools	Strains		Epilepsy	Schizophrenia	Arthritis
Idiopathic Epilepsy	9	105	13	**68**	47	35
Schizophrenia	7	63	11	49	**72**	38
Chronic Arthritis	7	76	12	28	30	**55**

*The antiserums used were prepared in parallel manner by repeated intravenous and subcutaneous injection of appropriate dilutions of the respective heat killed (70°C. 1 hour) streptococci whose antigenic specificity was preserved throughout the long period of immunization (one and one-half years) in dense suspension (1,000,000,000,000 streptococci per ml.) in glycerine 2 parts and 25 per cent sodium chloride solution 1 part.

TABLE 3

AGGLUTINATION OF STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY THE UNABSORBED AND ABSORBED SERUM OF HORSES IMMUNIZED WITH THE RESPECTIVE STREPTOCOCCI.

Source of Streptococci	Streptococcal		Experiments	Percentage of total possible agglutination at fivefold dilutions of 1-20 to 1-2,500 of the unabsorbed and absorbed serums of horses immunized with streptococci isolated in studies of											
				Epilepsy				Schizophrenia				Arthritis			
					Absorbed with streptococci isolated in studies of				Absorbed with streptococci isolated in studies of				Absorbed with streptococci isolated in studies of		
	Pools	Strains		Unabsorbed	Epilepsy	Schizophrenia	Arthritis	Unabsorbed	Schizophrenia	Epilepsy	Arthritis	Unabsorbed	Arthritis	Schizophrenia	Epilepsy
Epilepsy	1	11	1	**75**	**38**	56	44	31	25	25	25	31	38	38	38
	1	12	1	**75**	**31**	50	49	31	31	31	38	56	56	56	25
Schizophrenia	1	10	1	31	25	25	25	**69**	**31**	44	38	44	25	25	25
	1	12	1	38	31	19	25	**63**	**25**	44	31	44	38	44	44
Arthritis	1	30	1	44	31	44	25	31	31	31	13	**69**	**0**	44	38
	1	42	1	25	13	25	6	19	13	13	6	**63**	**0**	25	25

containing antibodies may be readily visualized and compared in the tables and text, the percentages of total possible agglutination in the four dilutions are given. A 4-plus agglutination in each of the four dilutions, or a total of 16, would be 100 per cent; a total of 5 pluses for the four dilutions would be 5/16, or 31 per cent, and so forth. This method was found to express more accurately the agglutinin titer of serums and of antibody solutions than did the end point at which agglutination occurred.

Interface precipitation tests were made in small glass tubes (5 x 25 mm.) by superimposing the solutions of specific polysaccharide of the respective streptococci obtained by the Lancefield method and the cleared NaCl solution washings of nasopharyngeal swabbings to which 0.2 per cent phenol had been added onto the undiluted serum of patients, on the serum of horses and rabbits that had been immunized with the respective streptococci, and on the solutions of the thermal antibodies to which 0.1

per cent agar or 1 per cent gelatin were added. The degree of clouding or precipitation at the interface, after thirty minutes at 35°C. and eighteen hours at 10°C., or after eighteen to twenty-four hours at 35°C. was recorded according to the arbitrary scale of 0 to 4 plus.

RESULTS OF CULTURES

Cultures on blood agar plates and some dilutions of cultures in dextrose brain broth or soft dextrose brain agar were made of nasopharyngeal swabbings from 181 persons suffering from epilepsy, from 258 persons suffering from schizophrenia, 85 persons suffering from either chronic or subacute arthritis, and, as a control, from 78 well persons. Green-producing colonies of alpha streptococci grew in greatly predominating numbers in most of the cultures and indifferent colonies in a few instances, never in predominating numbers. Variable numbers of colonies of Micrococcus catarrhalis and of staphylococci grew in most instances, and in no instance did Hemophilus influenzae grow in large numbers. There was no distinctive difference between the type of colonies that grew in the different groups. In general, however, the number of colonies was greater, often far greater, in the persons who were ill than in those who were well.

Shake cultures in blood agar and serial dilution cultures in dextrose brain broth or alternately in dextrose brain broth and dextrose brain agar were made from the spinal fluid in 24 individuals, from the urine in 10, from the apexes of pulpless teeth extracted in a sterile manner in 24, and from the stool in 23 persons suffering from schizophrenia. The spinal fluids proved sterile; greening streptococci were isolated in small numbers from the urine, and in large numbers from the teeth; and greening or indifferent streptococci were isolated in 19 of the 23 stools cultured.

Cultures in the dextrose brain broth of the partially macerated blood clot yielded highly pleomorphic greening or indifferent streptococci to blood agar in 49, or 29 per cent, of 161 persons suffering from epilepsy, in only 5, or

TABLE 4

AGGLUTINATION OF ALPHA STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY THE SERUM OF RABBITS BEFORE AND AFTER IMMUNIZATION WITH THE RESPECTIVE STRAINS OF STREPTOCOCCI.*

Source of Streptococci	Streptococcal		Percentage of total possible agglutination by the serum of rabbits at fivefold dilutions, 1-20 to 1-2,500 before and after immunization with streptococci isolated in studies of							
			Epilepsy		Schizophrenia				Arthritis	
			Rabbit 8		Rabbit 6		Rabbit 7		Rabbit 9	
	Pools	Strains	Normal	Immune	Normal	Immune	Normal	Immune	Normal	Immune
Epilepsy	1	15	0	**56**	13	19	0	25	0	19
	1	16	19	**81**	25	50	25	50	13	38
	1	17	0	**56**	6	13	19	25	0	0
Total	3	43	6	**64**	15	27	15	33	4	19
Schizophrenia	1	10	19	38	25	**81**	25	**63**	19	25
	1	8	25	44	25	**88**	25	**88**	25	38
	1	18	13	25	25	**56**	19	**63**	13	25
Total	3	36	19	36	25	**75**	23	**71**	19	29
Arthritis	1	31	13	25	19	31	6	25	13	**56**
	1	31	19	25	13	19	6	19	0	**63**
	1	65	13	0	0	19	0	6	6	**56**
Total	3	96	15	17	11	23	4	17	6	**58**

*The antiserums used were prepared in parallel manner by three daily intravenous and subcutaneous injections per week for four weeks of the respective heat killed (65°C. 1 hour) streptococci. The rabbits were bled before the first and ten days after the last injection and the agglutination tests were done ten days after the immunized rabbits were bled.

TABLE 5

AGGLUTINATION OF STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY THE UNABSORBED AND ABSORBED SERUMS OF RABBITS THAT HAD BEEN IMMUNIZED WITH THE RESPECTIVE STREPTOCOCCI.

Source of Streptococci	Streptococcal		Percentage of total possible agglutination of respective streptococci by the serums of rabbits at fivefold dilutions of 1-20 to 1-2,500 immunized with the streptococci isolated in studies of								
			Epilepsy			Schizophrenia			Arthritis		
			Rabbit 8			Rabbit 6			Rabbit 9		
	Pools	Strains	Unabsorbed	Absorbed with streptococci isolated in studies of		Unabsorbed	Absorbed with streptococci isolated in studies of		Unabsorbed	Absorbed with streptococci isolated in studies of	
				Epilepsy	Arthritis		Schizophrenia	Arthritis		Arthritis	Epilepsy
Epilepsy	1	15	**75**	**31**	44	25	25	25	31	31	31
	1	16	**69**	**44**	63	50	50	50	50	38	31
Schizophrenia	1	10	50	44	44	**69**	**38**	56	31	25	25
	1	8	50	38	44	**69**	**38**	63	50	50	44
Arthritis	1	31	25	19	19	25	19	19	**50**	**6**	44
	1	65	25	19	19	25	19	19	**50**	**0**	31

4 per cent, of 125 persons suffering from schizophrenia, in 7, or 14 per cent, of 69 persons having chronic arthritis, and in not one of 62 well persons or persons suffering from noninfectious ailments. The incidence of isolation of streptococci from the blood in persons having epilepsy was highest shortly before or during seizures, and most of the 49 persons from whose blood the streptococcus was isolated were taking phenobarbital or dilantin or both at the time the blood was drawn.

RESULTS OF AGGLUTINATION EXPERIMENTS

The type of agglutination experiments which were done, the way results were recorded, and the method of determining the percentage of agglutination and of indicating specificity are shown in *Table 1*. The results of agglutination of a large number of the respective strains by the different antiserums, by thermal antibodies, and by the serum of patients are summarized in *Tables 2, 4, 6, 7, and 8*. A high degree of respective specific agglutination was obtained with

TABLE 6

AGGLUTINATION OF ALPHA STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY THERMAL ANTIBODY PREPARED FROM THE RESPECTIVE STRAINS OF STREPTOCOCCI, 20,000,000,000 PER ml. IN NaCl SOLUTION, AUTOCLAVED FOR 96 HOURS.

Source of Streptococci	Streptococcal		Agglutination Experiments		Antibody preparations	Percentage of total possible agglutination at fivefold dilutions of 1-20 to 1-2,500 of thermal antibody prepared from streptococci isolated in studies of		
	Pools	Strains	number	time		Epilepsy	Schizophrenia	Arthritis
Epilepsy	1	11	8	1945	4	**50**	30	0
	1	12	6	1946	5	**44**	25	0
Schizophrenia	1	10	9	1945	4	38	**50**	0
	1	15	7	1946	5	38	**63**	13
Arthritis	1	30	7	1945	4	38	38	**50**
	1	12	8	1946	5	31	38	**56**

TABLE 7

AGGLUTINATION OF ALPHA STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA, ARTHRITIS AND RESPIRATORY INFECTIONS BY THERMAL ANTIBODY PREPARED FROM THE RESPECTIVE STRAINS OF STREPTOCOCCI, 10,000,000,000 PER ml. IN NaCl SOLUTION PLUS 1.5% H_2O_2 AND AUTOCLAVED FOR ONE HOUR.

SOURCE OF STREPTOCOCCI	STREPTOCOCCAL		PERCENTAGE OF TOTAL POSSIBLE AGGLUTINATION AT FIVEFOLD DILUTIONS OF 1-20 TO 1-2,500 OF THERMAL ANTIBODY PREPARED IN VITRO FROM STREPTOCOCCI ISOLATED IN STUDIES OF							
			EPILEPSY (10)*		SCHIZOPHRENIA (14)		ARTHRITIS (5)		RESPIRATORY INFECTIONS (8)	
	POOLS	STRAINS	Tests	Per cent Agglutination	Tests	Per cent Agglutination	Tests	Per cent Agglutination	Tests	Per cent Agglutination
EPILEPSY	13	83	39	**63**	48	53	6	38	14	52
SCHIZOPHRENIA	13	118	42	47	67	**68**	6	45	19	47
ARTHRITIS	3	44	21	40	28	35	8	**73**	12	50
RESPIRATORY INFECTIONS	8	175	23	48	26	51	7	38	17	**73**

*Figures in ( ) indicate the number of preparations of thermal antibody used in the agglutination tests.

TABLE 8

AGGLUTINATION OF STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA, ARTHRITIS AND RESPIRATORY INFECTIONS BY THE SERUMS OF PERSONS SUFFERING FROM EPILEPSY, SCHIZOPHRENIA OR ARTHRITIS AND OF WELL PERSONS.

SOURCE OF STREPTOCOCCI	STREPTOCOCCAL		EXPERIMENTS		PERCENTAGE OF TOTAL POSSIBLE AGGLUTINATION OF RESPECTIVE STREPTOCOCCI AT FIVEFOLD DILUTIONS OF 1-20 TO 1-2,500 OF THE SERUM OF PERSONS SUFFERING FROM			
	POOLS	STRAINS	NUMBER	TIME OF	EPILEPSY (137)*	SCHIZOPHRENIA (108)	ARTHRITIS (53)	CONTROL WELL PERSONS (59)
EPILEPSY	2	23	9	1945	**64**	45	19	20
	10	133	30	1946	**58**	35	12	15
SCHIZOPHRENIA	2	22	9	1945	45	**68**	26	19
	6	58	23	1946	42	**60**	25	13
ARTHRITIS	2	43	9	1945	14	19	**53**	16
	4	43	14	1946	10	10	**37**	13
RESPIRATORY INFECTIONS	3	115	4	1945	22	18	27	36

*The figures in ( ) indicate the number of patients whose serum was used. About one-half were tested in 1945 and 1946 respectively. However, the agglutinating action of the former group was determined in pools of 4-6 while that of the serums of the latter group was determined separately.

TABLE 9

AGGLUTINATION OF STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY THE UNABSORBED AND ABSORBED SERUMS OF RESPECTIVE PATIENTS AND BY THERMAL ANTIBODY.

SOURCE OF STREPTOCOCCI	STREPTOCOCCI		EXPERIMENTS		PERCENTAGE OF TOTAL POSSIBLE AGGLUTINATION AT FIVEFOLD DILUTIONS OF 1-20 TO 1-2,500 OF SERUM OF PATIENTS SUFFERING FROM									THERMAL ANTIBODY PREPARED FROM STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY		
					EPILEPSY			SCHIZOPHRENIA			ARTHRITIS					
	POOLS	STRAINS	NO.	TIME	UNABSORBED	ABSORBED WITH STREPTOCOCCI ISOLATED IN STUDIES OF		UNABSORBED	ABSORBED WITH STREPTOCOCCI ISOLATED IN STUDIES OF		UNABSORBED	ABSORBED WITH STREPTOCOCCI ISOLATED IN STUDIES OF		UNABSORBED	ABSORBED WITH STREPTOCOCCI ISOLATED IN STUDIES OF	
						Epilepsy	Arthritis		Schizophrenia	Arthritis		Arthritis	Epilepsy		Epilepsy	Arthritis
EPILEPSY	2	23	2	1945	**56**	**13**	38	38	13	25	25	13	13	**63**	**44**	50
	1	11	1	1946	**69**	**13**	38	50	38	25	.....	.....	.....	**69**	**56**	.....
SCHIZOPHRENIA	2	21	2	1945	25	13	25	**54**	**0**	38	0	13	13	50	44	31
	1	10	1	1946	38	25	25	**57**	**19**	38	.....	.....	.....	31	31	.....
ARTHRITIS	2	43	2	1945	19	25	19	19	25	13	**56**	**13**	38	44	**44**	**31**
	1	30	1	1946	25	25	13	38	25	13	.....	.....	.....	44	31	.....

TABLE 10

AGGLUTINATION OF STREPTOCOCCI AND PRECIPITATION OF STREPTOCOCCAL POLYSACCHARIDE BY THE SERUM OF PERSONS SUFFERING FROM EPILEPSY IN RELATION TO GRAND MAL SEIZURES.

Source of Streptococci	Streptococcal		Percentage of total possible agglutination of the respective streptococci at fivefold dilutions of 1-20 to 1-2,500 of the serum of persons suffering from epilepsy obtained shortly before and after grand mal seizures.									
			Case 1		Case 2		Case 3		Case 4		Case 5	
	Pools	Strains	B*	A*	B	A	B	A	B	A	B	A
Epilepsy	1	11	44	**69**	56	**63**	44	**56**	38	**63**	56	**81**
Schizophrenia	1	10	31	50	25	38	31	44	38	50	38	50
Arthritis	1	30	38	31	0	0	25	13	13	25	25	25
Encephalitis	1	24	38	25	0	0	38	25	13	38	31	31
Respiratory Infections	1	95	31	38	25	13	25	13	0	13	31	31
Peptic Ulcer	1	12	31	13	0	0	13	25	0	13	13	13
			Percentage of precipitation of respective streptococcal polysaccharide.									
Epilepsy	1	11	25	**50**	50	**50**	25	**50**	25	**50**	50	**75**
Schizophrenia	1	10	0	25	25	25	25	25	0	25	25	25
Arthritis	1	30	0	0	25	25	0	25	0	25	25	25

*B► 1–3 hours before seizures. A► 1–3 hours after seizures. The degree of precipitation was recorded according to the arbitrary scale of 0–4 plus, each plus representing 25 per cent.

each of the different types of antiserums, with the thermal antibody, and with the serum of the patients.

The results of experiments on specificity of agglutinins by absorption from the respective serums and thermal antibody with homologous and heterologous streptococci are summarized in *Tables 3, 5, and 9.* It will be seen that absorptions with the homologous strains consistently caused a far greater reduction of agglutinins than heterologous strains. Moreover, the reduction was usually relatively greater by the more closely related heterologous strains isolated in studies of epilepsy and schizophrenia, respectively, than by more distantly related strains isolated in studies of arthritis.

Thermal antibody, the serums of horses and rabbits that had been immunized with the respective streptococci, and the serum of persons all agglutinated specifically the streptococci isolated from nasopharynx, apexes of pulpless teeth, and blood, but did not agglutinate the streptococci isolated from the urine and feces.

The agglutinin titers of the serums of patients suffering from epilepsy shortly before and shortly after grand mal seizures over streptococci isolated in studies of different diseases and precipitation of polysaccharide obtained from streptococci isolated in studies of epilepsy, schizophrenia, and arthritis are summarized in *Table 10.* It will be seen that the agglutinin and precipitin titers were consistently higher with the serum obtained shortly after seizures than with the serum obtained shortly before seizures. This was associated with a sharp drop in specific streptococcal antigen in skin or blood determined by intradermal injection of antibody (to be reported elsewhere).

RESULTS OF PRECIPITATION EXPERIMENTS

The results of precipitation experiments with the antiserums prepared in rabbits and horses, the serum of patients, and the two types of thermal antibodies over different dilutions of polysaccharide of the respective streptococci are summarized in *Tables 11, 12, and 13,* and those obtained with antiserum of horses, rabbits, and serum of patients over cleared sodium chloride solution washings of nasopharyngeal swabbings are shown in *Table 14.* A high degree of specificity was consistently obtained with each of the materials containing antibody.

COMMENTS AND SUMMARY

The results of agglutination and precipitation experiments with suspensions, extracts,

and solutions of polysaccharide of alpha streptococci isolated in studies of idiopathic epilepsy, schizophrenia, and as controls in arthritis, and the serum of respective patients, the serum of horses and rabbits that had been immunized with the respective streptococci, and thermal antibodies prepared in vitro from streptococci isolated in studies of epilepsy, schizophrenia, and arthritis are reported.

A consistently high degree of specific agglutination of the respective streptococci and of specific agglutinin absorption and a correspondingly high degree of specific precipitation of extracts of the streptococci, of extracts of nasopharyngeal swabbings, and of solutions of polysaccharide by the serums of patients, by the serums of immunized horses and rabbits, and by thermal antibody were obtained.

The streptococci subjected to the serologic tests were isolated chiefly during studies of the past two years, but some were taken as long as twelve years before from nasopharyngeal swabbings, from infected teeth, and from the blood of widely separated groups of persons suffering from the respective diseases.

Success in separating the specific types of alpha streptococci from saprophytic types normally present in nasopharynx of human

TABLE 11

PRECIPITATION REACTION BETWEEN THE SERUM OF RABBITS IMMUNIZED WITH STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS AND THE POLYSACCHARIDE OF THE RESPECTIVE STREPTOCOCCI.

SOURCE OF STREPTOCOCCI	SOLUTION OF POLYSACCHARIDE FROM 50 BILLION STREPTOCOCCI PER ml. OF FOLLOWING POOLS OF STREPTOCOCCI			PRECIPITATION (0–4) AT THE INTERFACE BETWEEN SOLUTIONS OF POLYSACCHARIDE OF STREPTOCOCCI AND THE SERUM OF RABBITS IMMUNIZED WITH STREPTOCOCCI ISOLATED IN STUDIES OF							
				EPILEPSY		SCHIZOPHRENIA				ARTHRITIS	
				RABBIT 8		RABBIT 6		RABBIT 7		RABBIT 9	
	POOLS*	STRAINS	DILUTION	Normal	Immunized	Normal	Immunized	Normal	Immunized	Normal	Immunized
EPILEPSY	844	46	1–0	0	**3**	0	1	0	2	0	2
			1–10	.....	**1**	0	0	.....	0	.....	1
			1–100	.....	**1**	0	0	.....	0	.....	0
	1075	16	1–0	0	**3**	0	1	0	2	0	1
			1–10	.....	**2**	0	1	.....	1	.....	1
			1–100	.....	**2**	0	0	.....	0	.....	0
	144	12	1–0	0	**3**	0	2	0	1	0	1
			1–10	.....	**2**	0	0	.....	0	.....	0
			1–100	.....	**1**	0	0	.....	0	.....	0
SCHIZOPHRENIA	845	28	1–0	0	1	0	**4**	0	**3**	0	1
			1–10	.....	0	0	**2**	.....	**2**	.....	0
			1–100	.....	0	0	**1**	.....	**1**	.....	0
	896	11	1–0	0	2	0	**4**	0	**4**	0	2
			1–10	.....	1	0	**1**	.....	**3**	.....	0
			1–100	.....	0	0	**1**	.....	**2**	.....	0
	146	12	1–0	0	2	0	**4**	0	**4**	0	1
			1–10	.....	1	0	**2**	.....	**2**	.....	1
			1–100	.....	0	0	**1**	.....	**2**	.....	0
ARTHRITIS	864	31	1–0	0	1	0	2	0	2	0	**3**
			1–10	.....	1	0	1	.....	1	.....	**2**
			1–100	.....	0	0	0	.....	0	.....	**1**
	862	1	1–0	0	1	0	2	0	2	0	**4**
			1–10	.....	1	0	2	.....	2	.....	**3**
			1–100	.....	0	0	0	.....	0	.....	**2**
	5592	12	1–0	0	1	0	2	0	1	0	**3**
			1–10	.....	1	0	0	.....	1	.....	**2**
			1–100	.....	0	0	0	.....	0	.....	**1**
CONTROL NaCl SOLUTION			1–0	0	0	0	0	0	0	0	0

*Figures indicate laboratory number of respective pools.

beings is attributable to the serial dilution methods used in the primary isolations. The maintenance of respective original specificity for agglutination and precipitation studies, for the preparation of specific antiserums, and also for production of thermal antibodies with heat alone, or with hydrogen peroxide and much less heat, is attributable to the preservation of specific properties of freshly isolated streptococci in dehydrated form in the dense suspension of glycerine, 2 parts and saturated sodium chloride solution, 1 part. Viability and specific virulence were often maintained for as long as two years in this menstruum, and antigenic specificity was maintained apparently indefinitely. In extended studies of alpha streptococci as isolated in studies of various diseases we have not been able to find a medium which will maintain viability, elective localizing power, or virulence, and specific serologic properties over prolonged periods. From these studies it became apparent that dormancy of cultures kept under proper conditions is especially favorable for maintaining viability and specific properties. Keeping cultures frozen in dry ice or in dehydrated form in vacuo on glass beads, although a usually satisfactory method, is cumbersome and not suited for routine studies. Viability of cultures of the respective streptococci was maintained for several years at room temperature without transfer in autoclaved chick embryo medium in tall columns layered with liquid petrolatum; however, changes in virulence and antigenicity occurred seasonally in accord with epidemics of respiratory and other injections.

Viability and antigenic specificity but usually not virulence were maintained in cultures of streptococci and pneumococci on blood agar slants sealed with sterilized paraffined corks or screw caps when stored at room temperature in the dark for years without transfer. Here also dormancy and reduced oxygen tension are

TABLE 12

PRECIPITATION REACTION BETWEEN THE SERUMS OF HORSES IMMUNIZED WITH STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS, THE SERUM OF PERSONS SUFFERING FROM THESE DISEASES AND THE POLYSACCHARIDE OF THE RESPECTIVE STREPTOCOCCI.

Source of Streptococci	Solution of polysaccharide from 50 billion streptococci per ml. of following pools of streptococci			Precipitation (0-4) at the interface between solutions of polysaccharide and the serum of					
				horses immunized with streptococci isolated in studies of			persons suffering from		
	Pools*	Strains	Dilution	Epilepsy	Schizophrenia	Arthritis	Epilepsy	Schizophrenia	Arthritis
Epilepsy	844	46	1–10	**3**	2	2	**2**	0	0
			1–100	**2**	1	1	**1**	0	0
	1075	16	1–10	**3**	1	2	**1**	0	0
			1–100	**2**	0	1	**1**	0	0
	144	12	1–10	**4**	1	2	**2**	0	0
			1–100	**2**	0	1	**2**	0	0
Schizophrenia	845	28	1–10	2	**2**	1	0	**1**	0
			1–100	0	**1**	0	0	**1**	0
	896	11	1–10	2	**2**	1	0	**2**	0
			1–100	0	**1**	0	0	**0**	0
	146	12	1–10	1	**3**	1	1	**1**	0
			1–100	0	**2**	1	0	**1**	0
Arthritis	846	31	1–10	2	1	**4**	0	1	**0**
			1–100	1	0	**2**	0	0	**1**
	862	1	1–10	2	1	**3**	0	0	**0**
			1–100	1	0	**2**	0	0	**1**
	5592	12	1–10	2	2	**4**	0	0	**1**
			1–100	1	0	**2**	0	0	**1**
Control NaCl solution			1–10	0	0	0	0	0	0

*Figures indicate laboratory number of respective pools.

important. The overlying gas in sealed blood agar slant cultures became rich in carbon dioxide. When carbon dioxide was displaced with atmospheric oxygen on breaking the seal while making subcultures, death of the surviving organisms usually occurred promptly.

The data obtained in this study and those obtained in the experiments on animals with the freshly isolated strains and those of cutaneous tests made with natural and thermal streptococcal antibodies and antigen (to be reported elsewhere) indicate that (1) persons suffering from epilepsy and schizophrenia, despite the usual absence or slight symptoms of an active infection, harbor in their nasopharynx, apexes of pulpless teeth, and sometimes in their blood specific types of alpha streptococci which are not harmless or casual invaders but which are specifically antigenic; (2) the streptococci and the "neurotoxins" which they produce have predilection for certain structures in the brain, and (3) they may play an important role in the pathogenesis of epilepsy and schizophrenia. Studies on the nature of the respective neurotoxins produced by the streptococci and the use of streptococcal vaccines and thermal antibodies in prevention and treatment are in progress at the present time.

TABLE 13

PRECIPITATION REACTION BETWEEN SOLUTIONS OF THERMAL ANTIBODY AND POLYSACCHARIDE PREPARED RESPECTIVELY FROM STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS.

FILTRATES OF SOLUTIONS OF POLYSACCHARIDE PREPARED FROM STREPTOCOCCI (50 BILLION PER ml.) ISOLATED IN STUDIES OF	STREPTOCOCCAL POOLS*	STREPTOCOCCAL STRAINS	DILUTIONS OF POLYSACCHARIDE	PRECIPITATION AT INTERFACE BETWEEN POLYSACCHARIDE OF STREPTOCOCCI AND FILTRATES OF THERMAL ANTIBODY PREPARED FROM STREPTOCOCCI ISOLATED IN STUDIES OF EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS BY AUTOCLAVING THE RESPECTIVE NaCl SOLUTION SUSPENSIONS FOR NINETY-SIX HOURS (20 BILLION PER ml.)			ONE HOUR + 1.5% H_2O_2 (10 BILLION PER ml.)		
				Epilepsy	Schizophrenia	Arthritis	Epilepsy	Schizophrenia	Arthritis
EPILEPSY	844	46	1-0	**1**	0	0	**2**	1	0
			1-10	**1**	2	1	**2**	1	0
			1-100	**2**	1	1	**3**	1	0
	1075	16	1-0	**1**	1	0	**3**	2	0
			1-10	**2**	1	1	**2**	1	0
			1-100	**1**	0	0	**1**	0	0
	144	12	1-0	**2**	1	0	**3**	2	0
			1-10	**2**	1	1	**2**	1	1
			1-100	**1**	0	0	**1**	0	0
SCHIZOPHRENIA	845	28	1-0	1	**2**	0	3	**3**	1
			1-10	1	**3**	1	1	**2**	0
			1-100	0	**2**	0	1	**2**	0
	896	11	1-0	1	**2**	0	3	**4**	1
			1-10	2	**3**	1	1	**2**	0
			1-100	1	**2**	0	1	**2**	0
	146	12	1-0	1	**3**	0	3	**4**	1
			1-10	1	**2**	1	1	**2**	1
			1-100	0	**1**	0	1	**2**	0
ARTHRITIS	864	31	1-0	1	1	**2**	2	2	**2**
			1-10	1	2	**2**	0	0	**0**
			1-100	1	1	**2**	0	0	**0**
	862	1	1-0	1	2	**3**	3	3	**2**
			1-10	1	1	**1**	0	0	**1**
			1-100	0	0	**1**	0	0	**1**
	5592	12	1-0	1	1	**1**	3	3	**1**
			1-10	1	1	**2**	1	1	**1**
			1-100	0	0	**1**	0	0	**1**

*Figures indicate laboratory numbers of respective pools.

TABLE 14

PRECIPITATION AT THE INTERFACE BETWEEN NaCl SOLUTION WASHINGS OF NASOPHARYNGEAL SWABBINGS OF PERSONS SUFFERING FROM EPILEPSY, SCHIZOPHRENIA AND ARTHRITIS AND THE SERUMS OF RESPECTIVE PATIENTS AND THE SERUMS OF HORSES AND RABBITS THAT HAD BEEN IMMUNIZED WITH THE RESPECTIVE STREPTOCOCCI.

SOURCE OF ANTIGEN: NASOPHARYNGEAL SWABBINGS	PERCENTAGE OF PRECIPITATION AT INTERFACE BETWEEN CLEARED NaCl SOLUTION WASHINGS OF NASOPHARYNGEAL SWABBINGS AND THE SERUM OF											
	HORSES IMMUNIZED WITH STREPTOCOCCI ISOLATED IN STUDIES OF				RABBITS IMMUNIZED WITH STREPTOCOCCI ISOLATED IN STUDIES OF				PERSONS SUFFERING FROM			
	Cases	Epilepsy	Schizophrenia	Arthritis	Cases	Epilepsy	Schizophrenia	Arthritis	Cases	Epilepsy	Schizophrenia	Arthritis
EPILEPSY	20	**65**	35	10	20	**85**	25	0	20	**70**	0	0
	21	**67**	38	14	.....	.....	.....	.....	.....	.....	.....	.....
	.....	.....	.....	.....	10	**80**	70	10	10	**40**	0	10
	17	**65**	29	0	.....	.....	.....	.....	17	**59**	.....	.....
	10	**70**	0	0	10	**50**	50	10	10	**70**	20	0
	68	**68**	32	7	40	**75**	38	5	57	**61**	4	2
SCHIZOPHRENIA	26	0	**58**	4	26	23	**69**	4	26	8	**62**	.....
	46	7	**72**	0	.....	.....	.....	.....	.....	.....	.....	.....
	10	0	**70**	0	.....	.....	.....	.....	10	0	**80**	.....
	20	10	**70**	5	.....	.....	.....	.....	20	10	**60**	.....
	102	5	**68**	2	26	23	**69**	4	56	7	**64**	2
ARTHRITIS	27	0	7	**41**	.....	.....	.....	.....	.....	.....	.....	.....
WELL CONTROLS	14	7	0	0	14	7	0	0	14	0	7	0
	34	3	0	0	.....	.....	.....	.....	.....	.....	.....	.....
	17	0	6	6	.....	.....	.....	.....	17	0	0	0
	20	0	0	0	20	15	10	5	20	10	0	0
	85	2	1	1	34	12	6	3	51	4	2	0

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Fluorine in Control of Children's Tooth Decay

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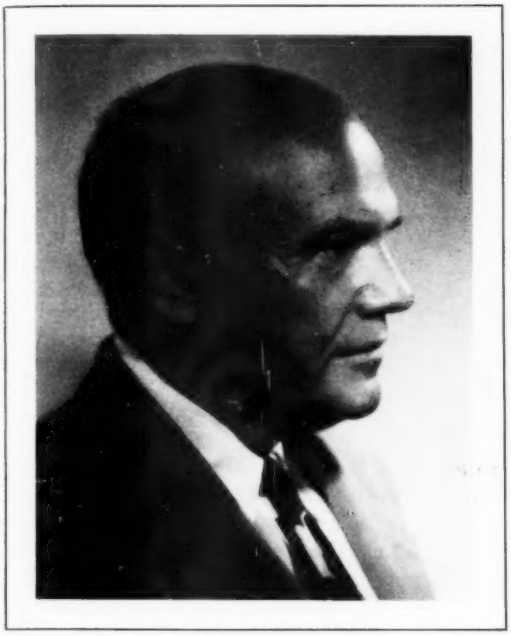
TOOTH decay is the most prevalent disease in the world. The recovered skulls of all ages except the Iron Age show teeth with decay. The Bronze Age skulls show 37 per cent with decay, whereas the skulls of the Roman colonists show 85 per cent.[1] Throughout the world today we see almost as much variation in groups living in different parts of the world. Polynesians in Samoa have shown 4 per cent with decay,[2] people in Tripolitania 50 per cent, and a group of children in Hawaii exhibited 99.9 per cent.[3]

Hawaii, with its mixed population, its warm, even climate, and the excellent medical control of the children on the sugar plantations, seemed an ideal place in which to study this problem. One study[4] showed 74 infants on a rice diet with 99.9 per cent with decay, and 50 per cent of all erupted teeth decayed. In a comparable group of 42 infants whose rice (acid residue starch) had been replaced by taro (a tuber with alkaline residue starch) only 7 per cent showed decay. Another group of 22 Polynesian children[3] living on a poi and fish diet had almost perfect teeth, whereas 55 Polynesians living in Honolulu, eating rice and bread, showed 98.2 per cent with decay. Ferguson recorded that decay was due to miscegenation, but the Island of Tristan da Cunha with 156 people of mixed races showed only 11 per cent with decay.[5]

In a study made in 1930, 779 Japanese children showed only two with noncarious mouths,[3] whereas at the same age in the same age group 109 Caucasian children showed 55.6 per cent with decay-free mouths. These children had much more fruit and vegetables and less cereal starches. The water was the same for both groups of children.

Because of certain dog experiments that seemed to verify the importance of the acid radicals in the diet,[6] it was assumed that the cause of decay was the excess of acid radicals in the food, since 50 per cent to 80 per cent of the calories came from acid residue rice. Another study made in 1937 seemed to confirm this.[7] A third study on 1140 children was made in 1940 to make a further check on the evidence presented.

The Dental Research Committee of the Honolulu Dental Association, consisting of 12 well-trained dentists, agreed to do the dental survey. Four main groups were studied. Group I consisted of approximately 250 children under the age of three, living on a plantation, who had been fed a well-balanced diet at the plantation health center every day for a period of seventeen years. The second group were the same type of children living eight miles away; these, however, had had no special feeding clinics. Group III consisted of specially selected



NILS P. LARSEN

children living on plantation No. 2 but coming from a higher economic bracket. Group IV consisted of 102 newly arrived Filipinos who were undernourished, anemic, and heavily infested with intestinal parasites. Examination showed very few of the latter children had firm muscles. The majority had distended abdomens and were definitely undersized compared with the local children. Yet the surprising fact was that their teeth were much better, with 89 per cent of their teeth being free of decay. This evidence suggested that a "good" or "bad" diet was not the answer, but that if certain elements were present in a diet, even though it was insufficient to produce good general health, tooth decay might be inhibited.

Of a group of 180 kindergarten children 55 per cent of the 3677 teeth were decayed, whereas of the 102 immigrant Filipinos only 11 per cent were decayed. Thirty-seven per cent of the teeth of the 278 Filipino children born and raised in Hawaii showed decay, and only 4.7 per cent of the mouths were entirely free of decay. On the other hand, 48 per cent of the newly arrived Filipinos' mouths were free of decay. Table 1 shows decay by races.

A careful diet check showed that the local Oriental diet was low in vegetables, legumes, fruits, milk, and even sweets, compared with a standard diet. It was high in cereals and proteins. At the health center 250 children under four years of age were fed a daily tuber, vegetable, and milk diet in place of the usual rice diet. In a study of the children on that plantation who were six years or younger, 66 per cent had perfect sets of teeth, and 87 per cent of all erupted teeth were decay-free. Of 127 children of the same age group on the nondiet plantation only 9 per cent had perfect sets and only 49 per cent of all teeth were free of decay. However, when a study was made of the chil-

TABLE 1

TOOTH DECAY BY NATIONALITIES

Nationality	Number of Children	Number of Decayed, Missing, Filled	Decay Free Teeth	Percent of DMF in All Teeth	Percent of Children Decay-Free
Japanese	556	6,565	6,525	50	1.0
Filipino	266	2,147	4,111	34	5.6
Miscegenetic	102	905	1,441	38	8.8
Chinese	44	430	552	43	6.3
Caucasian	44	286	641	31	11.3
Porto Rican	15	254	100	71	6.6
Korean	5	61	55	52	0.0
Hawaiian	4	68	28	70	25.0
New Filipinos	100	253	1,771	12	47.0
Totals	1,136	10,969	15,224	41	7.6

dren living on these two plantations who were six years old and over, it was revealed that 40.8 per cent of the teeth of those on the diet were decayed as compared to 41.6 per cent of the teeth of those who were not on a diet. This was a mathematically insignificant difference.

TABLE 2

	Group Given Calcium Fluoride		Control Group of 45 Children	
	Before Tablets	After Tablets	First Examination	Second Examination
Teeth with active decay	941	354	265	306
Teeth with nonactive decay	178	882	28	74
Decay-free teeth	805	721	385	411

It seemed evident that water alone—they all drank the same water—or sunshine alone—they all had seven and a half hours of sunshine daily—wasn't the factor. Heredity did not seem to be important because Oriental children on certain diets had good teeth and others on different diets had bad teeth. Filipinos in Hawaii had bad teeth, whereas newly arrived Filipinos had good teeth. The relation of the toothbrush to tooth decay seemed unimportant, since those with good or bad teeth performed this rite equally. The acid base factor alone did not seem to be the answer since many of the newly arrived Filipinos ate rice three times a day. It was a home-threshed rice, but acid residue. To stop eating candy is not the answer. Some high candy eaters have no decay, whereas many low sugar eaters have considerable decay. The California studies[8] showed that although an excess of sugar definitely seemed to increase the growth of lactobacilli, 10.4 teaspoons of sugar a day was used by the students with perfect teeth. In the experiment by Percy Howe[9] monkeys were fed adhesive sugar balls twice daily for eight months and they did not develop any dental caries.

Hence it seemed other factors might be responsible for the rampant tooth decay found. Recent studies[10] showed the water in Hawaii to be low in fluorine—0.02 parts per million to 0.2 parts per million. Other studies had shown that brackish water and fish foods[11,12] were high in fluorine. About this time (1945) the Navy put out a study on rats[13, 14] in which it was shown that oxalates gave a form of surface protection that apparently provided as much decay resistance as fluorine. The value of these two factors, fluorine and oxalates, which were unknown as possible controlling factors at the time of the previous studies, might prove to be as important as, or even more important than, the previously enunciated acid base factor.

To try to determine the effect of fluorine, a group of 180 kindergarten children were used for intensive study, since they had very rampant tooth decay (55 per cent). Rampant tooth decay is commonly seen in Hawaii in the deciduous teeth and is called odontoclasia. It is a rapidly spreading surface enamel decay that can be differentiated from ordinary caries, though the causes may be the same. One hundred and nineteen of these children were told to suck one calcium fluoride tablet a day (2.0 mg. calcium fluoride, 30.0 mg. vitamin C and 400 I.U.U.S.P.XII vitamin D*). The children were given these tablets over a period of about four months. Each child received an average of 98 tablets. The results are shown in Table 2.

The fact that the control group of 45 children were not receiving fluorine was known to the dentists. The figures seemed to show a striking difference. Apparently calcium fluoride tablets had caused a definite decrease in the activity. The dentists were quite convinced that the activity was decreased. How-

*Supplied through courtesy of Ayerst, McKenna & Harrison, Ltd.

Plantation Children

Dental survey being made in 1946 in the Health Center room of plantation.

ever, scattered among the children getting fluorine were some 24 children who did not receive the tablets. The dentists were unaware of this fact. Table 3 shows the results among this group.

TABLE 3

	First Examination	Second Examination
Teeth with active decay	181	58
Teeth with nonactive decay	25	123
Decay-free teeth	270	218

The fluorine cases showed a 37 per cent decrease in tooth decay activity, whereas the controls showed a 10 per cent increase. However, the unknown controls showed a decrease of 32 per cent. The findings suggest that the unconscious mind had considerable influence in deciding whether the tooth decay was active or nonactive. It indicates the need of careful and double controls for each conclusion reached.

The sputa examinations[15] also suggested that no definite change had been accomplished by the tablets. An analysis was made on more than one specimen from each child studied. Dr. Hartmann, Professor of Bacteriology at the University of Hawaii, used the color test to check the bacteriologic counts. We were forced to the conclusion that in the course of four months the use of one calcium fluoride tablet given daily (the present market price being $3 per hundred tablets) had failed to influence the lactobacillus count.

Fulton stated[16] that less than 1000 lactobacilli per cubic centimeter indicates immunity to tooth decay; counts up to 15,000, moderate susceptibility; the higher the counts, the greater the susceptibility. This is generally accepted as a good indication of the degree of susceptibility to caries.

Odontoclasia: A rapidly spreading surface enamel decay commonly seen in Hawaii.

The evidence did not seem to support the theory that one calcium fluoride tablet influenced tooth decay. The evidence, however, is overwhelming that children should get some fluorine, preferably as 1 part per million of sodium fluoride in their drinking water. Children who get this amount of fluorine have a caries experience rate of 240, whereas children living in cities in which the fluorine content of the water is as low as it is in Honolulu have a caries experience rate of 740.[17] Because of this inconclusive evidence some of the dentists are

TABLE 4

Lactobacillus Count	Fluorine Subjects		Nonfluorine Subjects		Unknown Controls	
	Before Tablets	After Tablets	First Examination	Second Examination	First Examination	Second Examination
High	87	81	25	19	18	11
Medium	19	26	4	12	4	4
Low	5	9	6	12	1	1

TABLE 5

1947 ENZIFLUR STUDY

		Control Subjects			Fluorine Subjects		
	St. Joseph	Comm. K.	Waipahu	Total	Comm. K.	Waipahu	Total
Deciduous Teeth							
Number of Children	A* 37	17	6	60	57	54	111
	B* 45	11	13	69	53	66	119
Number of Teeth	A 732	412	117	1261	1111	1055	2166
	B 869	219	252	1340	1005	1263	2268
Decay Free	A 385	228	42	655	480	325	805
	B 411	118	100	629	356	365	721
Decayed	A 293	143	63	499	529	577	1106
	B 384	69	114	567	531	683	1214
Missing	A 13	11	1	25	34	59	93
	34	3	9	46	51	80	131
Filled	A 41	30	21	92	68	84	152
	B 44	29	29	102	67	115	182
Active	A 265	119	62	446	407	534	941
	B 306	4	54	364	109	245	354
Nonactive	A 28	24	1	53	122	56	178
	B 74	63	60	197	422	460	882
Permanent Teeth							
Number of Teeth	A 19	8	3	30	65	59	124
	B 58	13	12	83	112	128	240
Decay Free	A 18	6	3	27	38	48	86
	B 53	9	7	69	85	100	185
Decayed	A 1	2	0	3	17	10	27
	B 5	4	2	11	26	24	50
Missing	A 0	0	0	0	0	0	0
	B 0	0	0	0	0	0	0
Filled	A 0	0	0	0	0	1	1
	B 0	0	3	3	1	4	5
Active	A 1	2	0	3	17	10	27
	B 5	2	2	9	5	23	28
Nonactive	A 0	0	0	0	0	0	0
	B 0	2	0	2	21	1	22
Sputa Color Test by Dr. Hartmann							
High	A 25	13	5	43	42	45	87
	B 19	4	7	30	34	47	81
Medium	A 4	4	0	8	12	7	19
	B 12	1	3	16	13	13	26
Low	A 6	0	1	7	3	2	5
	B 12	0	1	13	6	3	9

A*—First Exam
B*—Second Exam

now using a 2 per cent sodium fluoride solution to paint the teeth three times a year after thorough cleansing. It has been shown[18] that this alone will reduce tooth decay by 40 per cent. However, after a thorough review of the literature, Ast cautions, "Let us be patient to await conclusive evidence before we make up our minds on the merits of fluorine therapy."[19]

The present popular cola drinks with a *p*H of 2.6 which can readily etch enamel may be an added factor in increasing the decay tendency.[20] This added to the mouth of children who already have a very high aciduric count, with no protective factors such as fluorine or oxalate to inhibit the bacterial growth or to protect the enamel from the effect of acid, would be an added danger in a community where the water is low in fluorine and particularly in a climate like Hawaii which induces an increased intake of cold drinks. Acid residue food (such as rice) can produce a urine *p*H as well as a sputum *p*H of 4 to 4.5. This is an ideal medium for the lactobacilli, which are the only mouth bacilli that can thrive and produce acid down to a *p*H of 3.2.

To correct tooth decay by diet, the correction

must be quantitative, such as a change from large amounts of rice or bread to large amounts of taro, potatoes, or vegetables, or the optimum amount of the protective factors, must be present. The protective factors must inhibit aciduric bacteria or the enzymes, or neutralize the acid that is present. When such conditions prevail in the mouth, there is an increased immunity to decay. Present thinking should be directed towards these protective factors, and every child should be given the benefit of this current knowledge, but further observations are necessary before complete conclusions can be made.

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Relation of the Emotions to Physical Discomfort

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THE changes which occur in the type of medical practice which we now see and the emphasis which is laid on different diseases occurring over a long period of years add much to the interest in the practice of medicine. During my days in medical school, teaching emphasis was placed on such diseases as typhoid fever, pneumonia, scarlet fever, diphtheria, etc. Very little was said and not much was known about the disturbances of function occurring in the body as a result of emotional unrest.

In World War I the type of disease which caused the greatest concern was that resulting from infections, particularly pneumonia and influenza. In World War II we had an entirely different problem. The patient whose case is to be discussed illustrates quite well a type of psychosomatic individual whom we have seen quite commonly in the military service.

The patient, a young lady, complains of nausea and vomiting which have been present off and on since the age of five years; occasionally the nausea is most distressing, then it will be mild for a short time and frequently disappears for several months. During the years that she has had these symptoms she did not experience any great weight loss until quite recently, when her complaints became quite distressing; in about two months she lost 15 pounds. She states that her nausea comes at almost any time, particularly if she gets excited, and that with the nausea she very frequently vomits. The nausea has no relation whatever to meals. Emptying the stomach gives some subjective relief. She rarely has any pain except that which is associated with straining while vomiting. The patient exhibits certain physical characteristics of an undernourished, apprehensive, emotional person, which is in keeping with the history of her illness.

An understanding of this young lady's history furnishes the only possible means of establishing for her a satisfactory therapeutic program and gives the only possible approach to helping her solve her own difficulties. She is now 25 years old. She was born and raised in a small town near Chicago. Her parents are good people, although her heredity is none too good; her mother had a nervous breakdown at one time. The girl's own life has been not very happy. She was quite well until she was five years of age, at which time she was forced to have a sexual experience with a member of her own family. There was a recurrence of this on six or eight occasions, or until she reached the age of seven years. Following her first experience she de-

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veloped nausea, later vomiting, which gradually increased; at times the vomiting became so marked that she lost some weight. After the age of seven the sexual insults ceased, and no further experiences of this kind occurred until she was eighteen years of age, when similar episodes were forced on her through contact with another person unrelated to her.

The sexual experiences, in which she more or less unwillingly participated, were without gratification. After several of these latter episodes she again began to suffer with nausea, vomiting, and sufficient weight loss to cause her and her family some concern. However, with the cessation of visits from the male friend she gradually recovered, and there were no more such experiences until she was 20 years old. From the age of 20 to 21 she was forced by a boy friend to submit to sexual intercourse at frequent intervals, and such episodes were followed by the same emotional patterns as those which had occurred in the past, except that now after each sexual experience she also suffered lower abdominal pain. To relieve this pain her appendix was removed but the operation did not effect any permanent benefit.

However, about two years later, at the age of 23, she met a boy friend who became interested in her to a certain extent, and who as she says, was more considerate than some of the others. The girl indulged in intercourse with this new friend in order to satisfy him. She still maintained an impassive attitude but without the objections she had formerly experienced, undoubtedly because of the friendly interest and at times expressed devotion of this particular boy friend, and also because he was interested in helping to solve some of her problems, particularly those relating to her family. The last experiences during this particular period with the boy friend did not provoke any particular nausea or vomiting; nor did she have any considerable amount of abdominal pain.

She progressed reasonably well until January of 1942, when the boy friend was inducted into the Army. Since this separation she has been lonesome and without any great amount of sustained interest in anything, although she has had many different types of employment. She tried to be a nurses' aide, and also worked in a hospital for the care of the tubercular. She has changed jobs on frequent occasions, never being able to stay at any one for any considerable length of time because of persistent nausea and occasional vomiting.

JAMES E. PAULLIN

THE most recent attack began with renewed vigor, resulting from a rather acute emotional upset. Since then she has been nauseated, has vomited most of her food, and has lost 15 to 20 pounds in weight within a month or six weeks.

In order to evaluate the patient's complaints of nausea, vomiting, and weight loss, she has been most carefully studied from the physical standpoint. She has received a careful examination, including x-rays, laboratory, and chemical studies, none of which revealed any evidence of an organic disease. Her stomach is perfectly normal. The small intestines show nothing abnormal. The large bowel is quite normal except for a moderate amount of spasticity. The blood examination is entirely normal. She does show a moderate amount of fibrosis in the lung fields, but there is no evidence of an active tuberculosis. The heart is perfectly normal in size, shape, and position. The basal metabolic rate is normal. All the examinations that could be

made, both physical and with the help of the laboratory, demonstrate her to be quite healthy except for an underweight condition and the evidences of emotional instability.

The next question which concerns us is what kind of a girl is she? And of just what kind of material is she made? In studying patients of this type it is just as necessary to know what kind of a patient has the complaint as it is to know what kind of disease the patient has. Unless we are able to answer these questions it is almost impossible for us to establish a satisfactory method of treatment.

In order to answer the latter question let us go back and look into the family history and into her family life. We find that her family consisted of her father, mother, and four siblings. She is the oldest and doesn't get along particularly well with the other members. Her mother says she is like her father, undemonstrative and a little peculiar, and between the father and the daughter there was a considerable amount of friction. Her mother is more or less partial to her younger sister, who is good looking and affable. The patient feels that she is more or less out of the family picture.

Of considerable importance in reconstructing her emotional life is the fact that her father died in the early part of 1944 and that following his death, the patient showed not the slightest reaction whatsoever. The patient has felt all along that she must assume a considerable amount of responsibility for the family's welfare. She had to help her mother in doing the housework and in caring for the other children. She has also felt that although she has done a considerable amount of work and rendered a great deal of financial help towards taking care of the family needs, her efforts are not appreciated. What she has done was her duty, without appreciation or thanks from the other members of the family group.

This résumé gives you a general picture of the problems with which we have to deal in this case. The girl came under the care of Dr. Elsie Haug at her family physician's recommendation because she had been vomiting for such a long period of time and had suffered such an extreme weight loss that the members of her family had become uneasy about her. The patient volunteered the further information that since she had become so weak she dreams a good deal. All her dreams are more or less tragic, having to do with death, drowning, and other experiences of a similar kind. Curiously enough, certain colors, odors, and noises precipitate vomiting. Brown colors always nauseate her, and she cannot eat foods that have a brown color, such as gravies and chocolate in any shape or form. Noises, particularly if they are loud and sudden, will always bring on an attack of vomiting.

The patient exhibits certain reactions resulting from many types of psychic trauma. We see, first, a girl born into a household which is not too congenial. The father and mother were evidently at odds. Her inheritance was none too good since her mother had had a nervous breakdown. Being the oldest of the children, the patient felt a tremendous family responsibility, which she apparently assumed because it was in line of duty. Then followed, beginning when she was 5 years old, psychological and psychic insults with which she tried to cope without help either from the family or from others. These resulted in the development of various escape mechanisms which might justify or excuse her conduct, and finally came the triumph of the emotions in a general bodily upheaval, bringing the patient to us in her present state.

Help may be obtained in unravelling cases with such an emotional background as this by employing sodium amytal or similar drugs to bring into the open many problems buried in the subconscious mind. The use of sodium amytal in this case was most helpful in uncovering many of the details of the patient's past life which have already been given you.

Many years ago Cannon, his co-workers, and others demonstrated that bodily changes taking place in animals and in man, as a result of pain, hunger, fear, rage, and sexual excitement, correlate with changes occurring in the tension of the smooth muscle of the body, but in particular with that part in the gastrointestinal tract. This particular patient exhibits one of the most outstanding examples of what we would call, if you want a name for it, anorexia nervosa.

As a result of the extremely distressing type of psychic trauma which this girl had in her early

years, the autonomic nervous system has been made to feel excessive and unusual varieties of stimuli which have been thrust upon a person not too well suited for such experiences—experiences that have to do with sexual intercourse with men, with related colors, such as brown, and also with noises. Either one of the latter two experiences can precipitate an emotional stimulus which, through the activity of the sympathetic nervous system, induces an undue tension in the smooth muscle of her gastrointestinal tract. The stomach becomes extremely irritable, and as many of you know who use the fluoroscope in examining the stomachs of nervous people, the moment the barium meal enters this organ there frequently begins marked peristaltic activity; in those who have nausea we observe a wave beginning in the pars media of the stomach extending towards the fundus and towards the pyloric end and according to the violence of these waves there begins an uncomfortable sensation of nausea, or regurgitation of the meal into the esophagus, sometimes producing vomiting.

Along with disturbances such as this, these people often lose their appetites and suffer with abdominal discomfort which they describe as gas, or fullness in the epigastrium, and pain in the abdomen. This type of slow, nagging pain, which is so frequently observed in patients, has been interpreted as being due to chronic appendicitis, gallbladder, or various other physical defects, and these individuals are subjected to operative procedures which occasionally afford temporary relief.

Associated with these changes in the smooth muscles there are other disturbances of body functions which take place. There is an increase in the pulse and respiratory rates, in the blood pressure, and in the blood sugar. These are well-recognized physical reactions to an emotional stimulus which begins in the brain and is transmitted through the sympathetic or parasympathetic nervous system, not only to smooth muscles but also to the glands of internal secretion, affecting the pituitary, the thyroid, the pancreas, the gonads, and the adrenals.

This patient exhibits certain suggestive evidence of such an endocrine disturbance related to her emotional imbalance. Within the past two or three years the menstrual periods have shown definite changes; while still regular there has been a very considerable decrease in the amount of the flow. Many of you may recall patients who have developed hyperthyroidism as a result of emotional stress or strain. As a matter of fact, if one looks carefully and inquires into the personal history of practically every patient who shows any marked evidence of hyperthyroidism, it will be fairly easy to find an emotional upheaval which precipitated the thyrotoxicosis. We have seen patients with diabetes mellitus in whom emotional stress or strain either aggravates already existing glycosuria or precipitates its development.

As Honorary Consultant to the Surgeon General of The United States Navy, I had an opportunity of observing, during an official visit to the various United States naval hospitals on the West Coast, a goodly number of patients who were returned to this country with all the symptoms, the physical signs, and clinical findings of diabetes mellitus. These men on their arrival at our hospitals from foreign duty were taking from 20 to 50 units of insulin a day; after being in our hospitals and in more familiar surroundings, and being given an adequate diet, it was observed that many of them could reduce the amount of insulin taken, and some dispensed with its use altogether, resuming a general diet without showing glycosuria or hyperglycemia. Not all of them fall into this category, however, and it is possible that some who apparently recover from diabetes may later develop the true disease, even though at the time the insulin was discontinued there was no evidence whatever of their former trouble. It is also interesting to note that all those who showed this type of behavior had severe and unusual emotional experiences.

When the diagnosis is made and when the type of patient who has the disease is understood, the next problem that arises is, what can we do to help these patients? This is the problem which faces us not only with this girl but with hundreds of others. I am not a psychiatrist but I am a psychologist, and I believe I know how to talk common sense to people who have diseases of the type shown by this patient. It is possible to help her a great deal, as has already been clearly demonstrated, in that during a month of treatment she

has gained 10 pounds in weight and has a different outlook on life.

One of the greatest mistakes a physician can make is to tell this type of patient, "You haven't anything so much the matter with your stomach and intestines. All you need is to get something to do and you will snap out of it." Such a statement as this immediately lets the patient know that you, as the physician, are not familiar with her case, and she feels that you can be of little help in overcoming many of her objective symptoms which she has interpreted in terms of serious organic disease, because you lack a true understanding of just how she feels. The first step then in treatment is that you have a complete understanding of the patient and that the patient has confidence in the doctor who is willing to listen to her story and who will carefully plan a course for her to follow in seeking health.

The next step in such a rehabilitation program is to explain to the patient how her symptoms developed from this particular type of reaction, and to tell her that the symptoms of nausea and vomiting, fullness, abdominal discomfort are not caused by an ulcer in the stomach, by any disease of the gallbladder, by an infected tube or ovary or an appendix, or by any other disease in the abdominal cavity, but result from the fact that the stomach—which is composed of smooth muscle and which normally contracts in order to empty itself of its contents—has become extremely irritable from impulses constantly coming to it through the sympathetic nervous system, beginning in that portion of the brain which controls the normal action and behavior of the stomach, intestines, and large bowel. Through the emotions this controlling center tends to become either stimulated or depressed by impressions or suggestions of such nature as would bring to her subconscious mind any of the psychic trauma which she originally experienced. An immediate stimulus through the autonomic nervous system is transmitted, in an exaggerated manner, to her stomach which in turn causes it to go into a state of tension, and through this tension she experiences the different sensations of which she complains.

Then explain to her that she very soon will be able to recognize the beginning of these sensations before there is nausea, and since she understands the mechanism of its workings she no longer needs to be afraid of consequences that arise. She should say and believe that she is sufficiently well acquainted with these stimuli to remark, "Oh yes, I know what produces these sensations. I recognize the fact that I am nauseated, and I know that I might be that way for a short while, but it isn't going to down me, and I am going on with something else. I can overcome it and I will do so by developing a normal reaction to that which occurs in a normal mind and body."

I would also explain to her that because she has these various symptoms, the natural thing for her to do is to interpret the discomfort which she has in terms of her actual experiences. In other words, she commonly hears that anyone who has pain in the stomach, nausea, vomiting, and loss of weight probably has cancer. Sooner or later she develops the idea subconsciously that she has cancer, because she hears so much about it and as soon as she is convinced that she has misinterpreted these experiences through which she is going, then she has a fair chance of reconciling her thoughts with the explanation which is given her, and she begins on the road to recovery.

In closing, may I leave this thought with you in regard to this particular girl. First, the type of response which she has exhibited to emotional stimuli is a more or less common pattern. In other words, she has developed a behavior pattern in response to emotional stimuli which is more or less characteristic. To do her the most good we must destroy this pattern; she must be taught how to overcome it and how to remodel her life so that these emotional upsets will not recur. Such an accomplishment cannot be brought about with the use of drugs. It cannot be accomplished by performing many or various surgical procedures. It can't be done by telling her there is nothing the matter with her. You can help by sitting down and discussing her problems with her, by explaining them to her, and by assuring her that while such a method of treatment is going to take time, she will be amply rewarded in the end by being able to resume a normal, healthy, productive life.

CLINICOPATHOLOGIC CONFERENCE

An Obscure Anemia

FROM NICHOLS VETERANS ADMINISTRATION HOSPITAL*

HAROLD GORDON, M.D., EDITOR

CLINICAL ABSTRACT

The patient, a 51-year-old white male, was admitted March 17, 1947, because of profound weakness, numbness, and a tingling sensation in his extremities. These symptoms had appeared eighteen months before, when he was hospitalized elsewhere for "yellow jaundice" and was told that he had "anemia." The onset of his illness is quite vague, but apparently he has not been able to work since June 1946. Before that, he often had to take time off because of generalized weakness. He says he has been jaundiced many times (every three or four weeks) during the last fourteen years, but his history is not very reliable and he is unable to give details concerning the jaundice. Apparently the icterus was not accompanied by nausea or vomiting. He states that he has had fleeting, sharp precordial pain for fourteen years, and blurring vision, headaches, and transient edema for six to eight years. He had many infectious diseases during childhood, and has had three attacks of pneumonia during adult life. He has no complaints referable to the gastrointestinal tract.

He worked at an ammunition depot from 1943 to June 1946 (forty months), handling "Yellow D" and T.N.T. About four months after starting this work, he developed intense jaundice and claims his urine became dark yellow. He says he had recurrent attacks of jaundice afterwards and was very yellow when hospitalized in July 1946. He was kept in the hospital until the end of August, when he left unimproved. Afterwards he remained at home, never entirely well. He received "shots" while in the hospital and also some "pills." He says he lost weight and now weighs 154 (usual weight 200 pounds).

When admitted he appeared well nourished but chronically ill. His temperature, pulse, and respirations were normal. Blood pressure was 132/80. His skin had a slightly lemon-yellow tint. His tongue was smooth and reddened. His mucous membranes were pale. He had a soft systolic murmur, which was heard best at the apex. Vibratory sensation was absent in all extremities. There were no other abnormal sensory changes. Position sense and reflexes were normal, as were his vital capacity, venous pressure and circulation time. His liver and spleen were not palpable, and he had no palpable or visible masses in the abdomen. No free acid was present in the stomach contents, even after stimulation with histamine. Reticulocyte counts were as follows (in per cent): March 21, 1.9; March 22, 1.2; March 24, 2.3; March 25, 0.7; March 26, 2.5; March 27, 2.2; March 30, 3.4; March 31, 3.5.

On March 25, platelet count was 114,400; the icterus index was 6 units; and the Van den Bergh, direct, negative, and indirect, trace. On March 26, platelet count was 120,130. Hematocrit, March 20, was 26 per cent; mean corpuscular volume, 105 cu. micra; mean corpuscular hemoglobin concentration 32.5 per cent. On March 26, these values were 39.5 per cent, 134 cu. micra and 27.5 per cent, respectively. Fragility test (March 20): hemolysis began

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at 0.42 per cent and was complete at 0.28 per cent saline concentration (normal control, 0.44 per cent and 0.34 per cent, respectively). Morphologic studies of several blood smears showed considerable macrocytosis with slight anisocytosis, moderate poikilocytosis, and occasional polychromasia. The neutrophilic leukocytes showed polylobulation.

Sternal puncture (March 17) showed increased cellularity of the marrow, with an absolute increase of erythroid cells and an increase of macronormoblasts and megaloblasts. The myeloid cells were diminished, but not remarkable otherwise, and bone marrow giant cells were plentiful. Blood Kahn was negative.

LABORATORY REPORTS

	R.B.C.	Hb. (gm.)	W.B.C.	Differential	
				Neutros. (Pct.)	Lymphs. (Pct.)
March 17	2.57	9.5	7,000	54	46
March 20	2.47	8.5	6,700	53	46
March 26	2.93	10.5	8,100	47	46
March 31	3.56	11.0	7,300	33	67

Course—The patient received 30 units concentrated liver extract (Lederle), intramuscularly, on March 20 and 15 units on March 26. To date (March 31), there has been no obvious clinical or symptomatic improvement.

DISCUSSION

DR. BEARD: Did he have a gastrointestinal series?

RESIDENT: Yes. It was normal.

DR. BEARD: Clinically, this patient presents changes typical of Addison's pernicious anemia. He has the blood count, the color, the tongue changes, the neurologic manifestations—everything except the history. I talked to him a few minutes ago. He insisted that he had "yellow jaundice" frequently during the last fourteen years. He told me he became "yellow all over" and had light-colored stools, but no indigestion during those attacks. That is significant from the standpoint of diagnosis. Perhaps I can make that clearer by considering the anemias in a general way first.

I classify the anemias according to the *mechanism* involved rather than according to the morphology of the erythrocytes. Wintrobe, in his textbook on hematology, has grouped the anemias as macrocytic, normocytic, or microcytic. Others classify them as due to deficiencies of blood-forming substances, to disturbances in the marrow, or to hemolytic processes. I prefer a broader classification, based upon the pathologic physiology—anemia due to iron deficiency, to E.M.F. deficiency, to myelophthisic disturbances, to hemolysis, or to hypoplasia of the bone marrow. This classification considers the causes of the anemias and provides a clue to their management.

Applying the five possible mechanisms indicated above to this particular patient, we must decide whether he has a deficiency of E.M.F., whether he has chronic hemolytic anemia, or whether he has both. The differentiation of the two, by examining the bone marrow, is not always easy. In both types the marrow is hyperplastic, with a definite "left shift" of erythroid cells. The immaturity of the erythroid cells of the marrow is not as marked in chronic hemolytic anemia as in anemia caused by E.M.F. deficiency. In both conditions, however, the erythroblasts and megaloblasts are increased. But there is this difference—in chronic hemolytic anemia the *serial maturation* of the erythroid cells is not interfered with, so the marrow contains megaloblasts, erythroblasts, and normoblasts in approximately normal proportion, though in increased number, whereas in the anemia of E.M.F. deficiency, megaloblasts and erythroblasts are proportionately and absolutely more numerous than the normoblasts. In chronic hemolytic anemia the marrow shows regenerative hyperplasia of erythroid elements, and in E.M.F. deficiency there is a "maturation arrest" of the erythroid cells.

Clinically, patients with chronic hemolytic

anemia present a history of moderate anemia usually with recurrent attacks of jaundice over a long period of time. Acute hemolytic anemia is relatively easy to recognize; chronic hemolytic anemia may on the other hand, present quite a confusing picture. The latter condition causes some anisocytosis and poikilocytosis, and also occasionally macrocytosis of the red blood cells.

This patient shows nothing to substantiate a diagnosis of chronic hemolytic anemia. He has no splenomegaly, and we expect the spleen to be palpable at least. He has neither clinical or laboratory signs of jaundice. I have seen cases without jaundice, but they are rare. When he was admitted, his reticulocyte count was only 1.5 per cent. In my experience, reticulocytosis is even more of a cardinal sign than severe jaundice. All in all, then, I think we can rule out chronic hemolytic anemia and have to fall back on E.M.F. deficiency as the cause of his anemia.

Now E.M.F. deficiency may develop in any one of several ways. Faulty nutrition can be ruled out immediately on the basis of the patient's general appearance and his dietary history. Sprue can be eliminated with equal readiness. This leaves true Addisonian anemia and the so-called achrestic anemia. He did not respond to specific therapy the way most patients with Addison's anemia do, so he falls in the group called "refractory anemia."

Refractory pernicious anemia is a very interesting condition, but unfortunately no one knows very much about it. These patients have a marrow which, as far as I'm concerned, is indistinguishable from that seen in the usual case of pernicious anemia. It shows a definite megaloblastic arrest. Many of the patients have neurologic changes identical with those seen in pernicious anemia. Most of them have no hydrocholoric acid and are histamine refractory. They have all the signs and symptoms of pernicious anemia, except that they don't respond to liver therapy. The current literature has many references to this type of anemia, and it has been claimed that folic acid therapy will cause a satisfactory remission even when liver has no effect. Dr. Gordon and I were discussing that point, and he remarked that this patient, having been hospitalized some months ago, must have received adequate amounts of folic acid in his diet. I think that that is true and that if this man should respond to folic acid, he will probably require an enormous amount of it.

From the point of view of diagnosis, then, we have to classify this patient in the group of E.M.F. deficiency anemias. He has all the clinical and laboratory changes necessary for that diagnosis. He lacks only the ability to respond to specific therapy, so we have to place him in the special sub-group of "refractory pernicious anemia."

I was asked to say something about the management of patients with pernicious anemia. There is good evidence that the average human liver contains about 300 units of E.M.F. Unpublished experiments performed by Dr. Carl Moore of St. Louis show that about 85 to 90 per cent of large doses of liver extract is stored by the liver, both in normal and in anemic individuals. These two observations are important from the point of view of management of patients with pernicious anemia.

Our objective is to return an anemic patient to normal as rapidly as possible. Therefore, it is my practice to give one unit of E.M.F. per day, according to the recommendation of the Standardization Committee, plus about 300 units for reserve storage in the liver. In one case we were able to show that approximately 85 per cent of the extract is stored in the liver. We gave one patient 300 units of liver extract in one dose. Her blood remained perfectly normal for about nine months, without additional therapy. Then her red blood cells started to decrease, so we placed her on the standard dosage of 30 units a month and maintained her in excellent balance on that as a maintenance dose. That is pretty good evidence that she was able to store E.M.F. and to call upon it according to the needs of her body.

As far as we know, the bone marrow is not primarily at fault in pernicious anemia. It is merely altered for lack of the E.M.F. stimulus. Accordingly, it probably does not matter appreciably how the dosage of the liver extract is spaced, provided the patient receives a total of 300 units, plus the additional amount necessary to cover the hospitalization period. It may be given at the rate of 15 units a day, up to 300 or more units, or it may be

given at a rate of 30 units a week until the same total amount has been administered. It is largely a matter of convenience—the convenience of the patient and that of the physician. After a satisfactory total has been given, the patient merely needs a maintenance dose.

Obviously, it is essential to give an active extract. The highly refined extracts are very satisfactory. At one time it was felt that the relatively crude extracts contain substances of special value for patients with neurologic changes. That is no longer the general consensus—it is simply a matter of making an early diagnosis and of maintaining adequate therapy with a potent extract.

As to the value of folic acid in treating Addison's anemia, I do not like it as well as I do liver extract. It has only one advantage—ease of administration. A serious disadvantage is that it does not arrest or cure any neurologic changes. The current literature shows that fact very definitely, even though some patients do respond satisfactorily both neurologically and hematologically. There is also a psychologic factor: If you start a patient on folic acid and don't get a good response, it may be difficult to persuade him to change to liver therapy, because it is so much easier to take a pill than to submit to hypodermic medication.

In my opinion, folic acid is valuable chiefly in the very rare cases of sensitivity to liver extract, and as an adjunct to liver, so that the latter does not need to be given quite as frequently. Perhaps, also, folic acid therapy may have a definite place in the very occasional case which proves to be refractory to liver extract. In general, patients with pernicious anemia respond so exactly to the calculated dose of 1 unit of liver extra daily that other therapy is seldom indicated.

It will probably be necessary to "feel your way" in the management of this particular patient. We see refractory cases occasionally. Recently I had a patient whose clinical picture was very similar to this one. The reticulocyte response to liver was only 2.0 per cent in eight days. After eight more days on liver, plus 30 mg. of folic acid, his reticulocyte count was only 3.5 per cent. His erythrocyte count, however, is improving, just as is the patient's whose case we are discussing. In fact, the two cases are very similar; they differ in only one respect. The man we are discussing has slightly more manifest neurologic lesions. Both have a normal leukocyte count instead of a leukopenia, such as is usual in Addison's anemia.

Some years ago we had a patient who was diagnosed by Dr. Gordon as having "pernicious anemia of pregnancy." However, her anemia persisted after her child was born. I saw her regularly after Dr. Gordon went into the service. She never responded satisfactorily and eventually died in spite of receiving large doses of liver extract for more than four years. I don't know why these patients do not respond and no one, to my knowledge, has offered a satisfactory explanation.

DR. GORDON: When this patient was selected for discussion, I felt that he was a classical example of Addison's anemia. When I asked Dr. Beard to speak, I was so sure of the diagnosis that I suggested he should devote time to a general discussion of the management of patients with pernicious anemia. As it turned out, this patient failed to respond to liver therapy, the way most patients with pernicious anemia do. However, his atypical response has been to our advantage today, since it helped to channel the discussion into a consideration of the management of refractory macrocytic anemia, and the place of folic acid therapy. Smears of the sternal marrow and of the peripheral blood show morphologic changes characteristic of pernicious anemia. The erythrocytes are macrocytic and show poikilocytosis and anisocytosis.

The sternal marrow is hyperplastic, with the increased cellularity due to maturation arrest of the erythroid cells. The leukocytes are polylobed. He did not respond to liver therapy the way we expected. I have no more idea than Dr. Beard has, why liver has been ineffective. As you know, the expected reticulocyte response depends on the initial erythrocyte count. This was shown years ago by Castle and his co-workers. It is not necessary to carry the figures in your head, but for those who like to do so, memorize the figures 8,5,4,3,2,1, and ½; multiply these by the factor 7, and you then have the expected reticulocyte count for initial erythrocyte counts of 1, 1.5, 2, 2.5, 3, 3.5, and 4 million, respectively.

In view of what has been said, I'd like to ask Dr. Beard to tell us how these refractory cases respond to massive doses of liver, say a very large initial dose and subsequent amounts of 15 units twice weekly; also, how they respond to a combination of liver and reticulin.

DR. BEARD: I don't believe it is possible to predict how a particular patient will react. Accordingly, I believe it is good practice to try different combinations of therapy. It will be interesting to see how this man reacts to a combination of folic acid and liver, or a combination of liver and reticulin, perhaps even a combination of all three.

DR. GOTT (Chief of Medicine): I am greatly interested in what Dr. Beard has told us about recent investigations regarding the amount of E.M.F. necessary to saturate a depleted liver or, if you prefer, a depleted individual. Up to now, in trying to regulate the amount of therapy, we have been guided largely by the reticulocyte and erythrocyte responses of each patient. I never could see any advantage to giving daily injections, when equally satisfactory results could be obtained by therapy at less frequent intervals and it is much more convenient for the patient. It has been my practice to inject 30 units and have the patient return twice during the first week for a checkup. Patients with pernicious anemia improve subjectively, even before there is an adequate red cell response. This improvement is dramatic and even diagnostic. At the end of a week, after repeating the necessary laboratory studies, I inject another 30 units and instruct the patient to return once weekly. I continue injecting 30 units each week until the erythrocyte count is maintained at a satisfactory level. Then I give him a maintenance dose of 30 units every two to four weeks.

As TO this case, I am not sure that he is suffering from pernicious anemia. His leukocyte count is out of line and he is not responding in a typical manner to liver therapy. However, he has shown some response. If we assume that his admittance erythrocyte count was two and a half million—and that, according to our present information was probably correct—he has, after two weeks' therapy, a count of approximately a million more. That is not a bad response, so I propose to continue him on a dosage of 30 units twice a week until we have observed him long enough to see if he fits into the pattern of true pernicious anemia. Later, if indications arise, we may give him iron or folic acid. It will depend entirely on his general progress, on his clinical status, and on the results of continued laboratory studies.

RUTIN STUDY GRANT MADE

A RESEARCH grant for the study of rutin has been made to the University of Nebraska by The Smith-Dorsey Company, according to a recent announcement. The work will be under the direction of Dr. Harry Miller, director of the University's chemurgy project, a division of the College of Agriculture.

Dr. Miller intends to select varieties of buckwheat which are high in rutin content and conduct plant breeding studies in an attempt to develop a superior strain. He also intends to try a new method of extraction of rutin from the buckwheat plant.

TECHNIC OF THE OPERATION

For Free Composite Grafts of the Nipples in Mammaryplasty

A Scientific Exhibit from William Milton Adams, M.D.,
Memphis, Tennessee

The nipples and areolae may be dissected free under local anesthesia, thus reducing the time of the general anesthesia for amputation and shaping of the breasts, or, the breasts may first be amputated under general anesthesia and, while the remaining tissue is being shaped and the graft beds are being prepared, the nipple grafts may be dissected from the amputated portions of the breasts by an assistant. The latter method is preferable, in that less time is consumed in the operation. After the breasts are amputated and the incisions closed, the general anesthetic is discontinued and local anesthesia is used for preparation of the recipient areas and application of the grafts.

In estimating the amount of breast tissue to be excised, the age of the patient and the size and shape of the entire body should be taken into consideration. Parallel semilunar lines of incision are marked on the posterior and anterior surfaces of the breasts. The lower incisions are placed along the inferior margins of the submammary folds; if placed above the folds, they will be plainly visible after healing takes place. If the breasts extend into the axilla or laterally onto the chest wall, the lower incisions are carried upward into the subaxillary region, or lower down so as to be covered by the patient's brassiere.

The patient is then placed in the sitting position, in order to permit one to mold the contour of the breasts properly and to observe their position on the chest wall. When the shaping is completed, the subcutaneous tissues are brought together and sutured with No. OO plain catgut. It is important that the subcutaneous tissues be closed snugly; in the event of liquefaction of the fatty tissues beneath, this prevents exudation of oil through the skin margins and possible separation of the incision. If necessary, the shape of the breasts may be materially altered by the use of retention sutures of No. O plain catgut through the mammary tissue itself. The skin is closed with interrupted sutures of No. 1 Deknatel placed about one-half inch apart, and a continuous suture of No. OOO Deknatel silk.

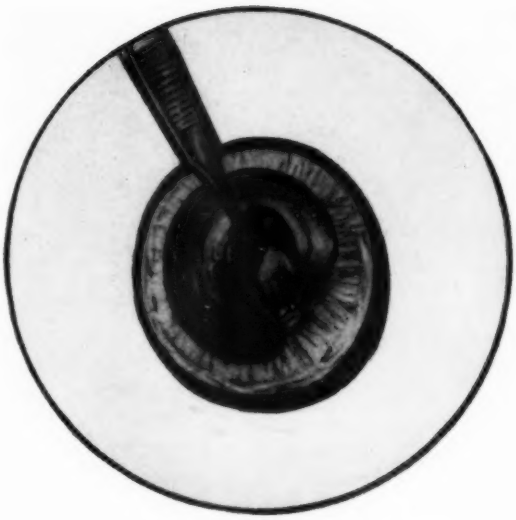
In all hypertrophied breasts, the areolae are also abnormally large, in some cases being as much as 5 inches in diameter. After the proper size is determined, dissection is begun at the periphery of the areola and carried toward the nipple as a free full thickness skin graft. As the nipple is approached, the dissection is gradually carried deeper to include a small amount of the smooth muscle tissue. Beneath the nipple itself, the incision is carried upward toward the surface in saucer fashion, to avoid making the graft too thick at this point. The nipple portion of the graft should be at least one-eighth inch thick in order to include a part of the smooth muscle tissue; it is not recommended, however, that any part of the graft be more than one-fourth inch in thickness.

The unused portion of the areolae of the amputated breasts are dissected free, wrapped in vaseline gauze and cellophane, and stored in the refrigerator for use in the event the nipple grafts themselves fail to take. One may use refrigerated skin grafts as late as ten days or two weeks postoperatively, with reasonable assurance of a satisfactory take. Although we have never lost a nipple graft, it is well to keep the additional areolar tissue as a precautionary measure.

After shaping of the remaining breast tissue is complete and the submammary incisions are closed, the patient is again placed in the sitting position and the sites for the nipple grafts are chosen. Recipient areas corresponding in size to that of the grafts are outlined, and the enclosed skin is dissected free to include almost the full thickness of the skin. One should avoid carrying the dissection so deep as to expose the subcutaneous fatty tissue, as this makes a poor surface for free grafting. The basal layer of the skin, having a rich blood supply, makes an ideal bed for the graft.

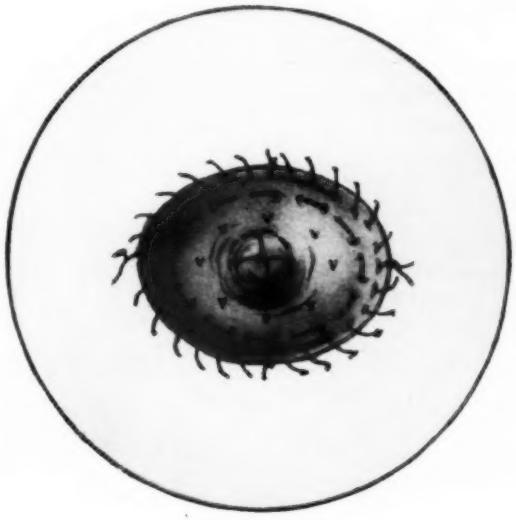
The nipple and areolar graft is evenly distributed over the recipient site and fastened in place with four diametrically opposed sutures. A continuous suture is then placed around the periphery. To insure perfect contact between the graft and its bed, and to prevent slipping of the graft and oozing of blood or serum from beneath, the entire nipple and areola are quilted to the basal layer of the skin with several rows of running stitch sutures. A dressing composed of one layer of rayon or vaseline gauze, a layer of dry gauze about one-eighth inch in thickness, and a layer of soft rubber sponge about one-fourth inch thick is placed over the nipple, the part of the rubber sponge which is directly above the nipple being saucerized to prevent undue pressure upon this elevated portion of the graft. Another thin layer of gauze is laid over the rubber sponge, and this part of the dressing is held in place with elastic adhesive. Layers of fluffy gauze are then applied over the entire breast and secured by an ace bandage around the chest. Part of the bandage should be carried over the shoulders to give an uplifting support. The importance of proper bandaging cannot be too strongly emphasized, since the success of the operation largely depends upon its application.

As a precaution against stitch scars, the large dressings and the submammary sutures are removed after six or seven days. Unless some complication arises, the dressings over the nipple grafts should not be disturbed for ten or twelve days.

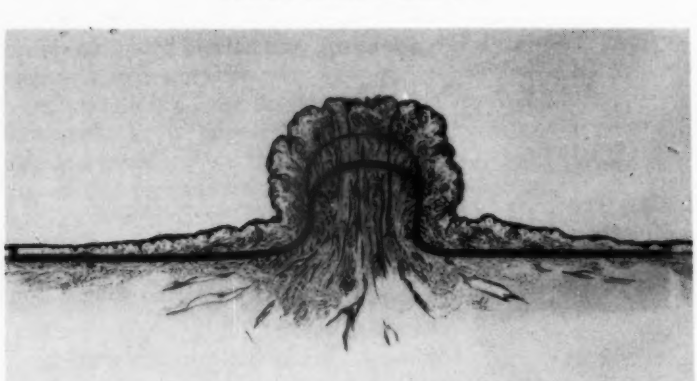


Left
Illustrating the dissection of the nipple and areola including a portion of the smooth muscle of the nipple.

Right
First step in the application of the nipple and areolar graft to its new location. Four retention sutures are used to insure an even distribution of the graft.

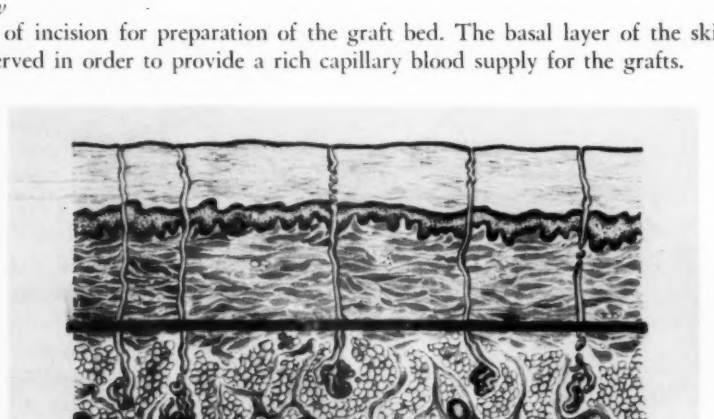


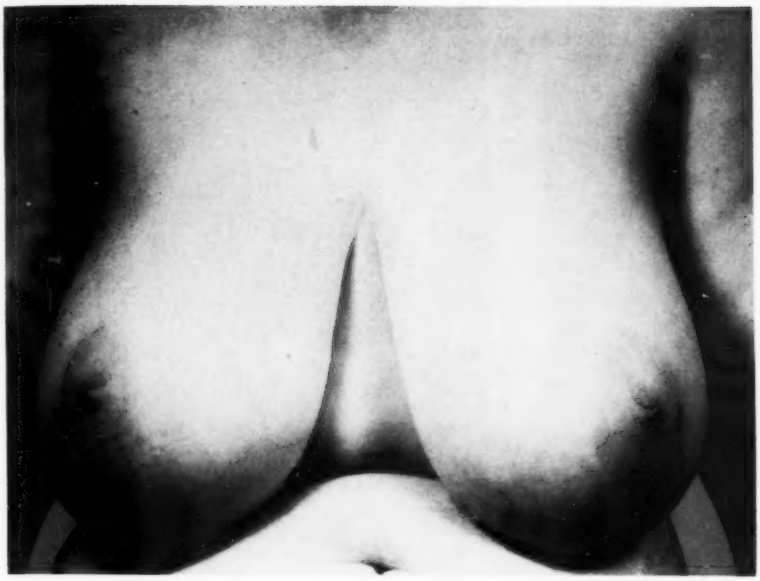
Left
Technic used in suturing the graft to its new site. A simple continuous suture is placed around the periphery. The central portion is quilted to the recipient area by running sutures.



Above
Incisions for removal of nipple and areolar grafts. The heavy line represents an incision approximately ¼ inch from the surface; this includes the maximum amount of smooth muscle which one should attempt to graft with the nipple. The lighter line represents an incision at a depth of ⅛ inch which includes the minimum amount.

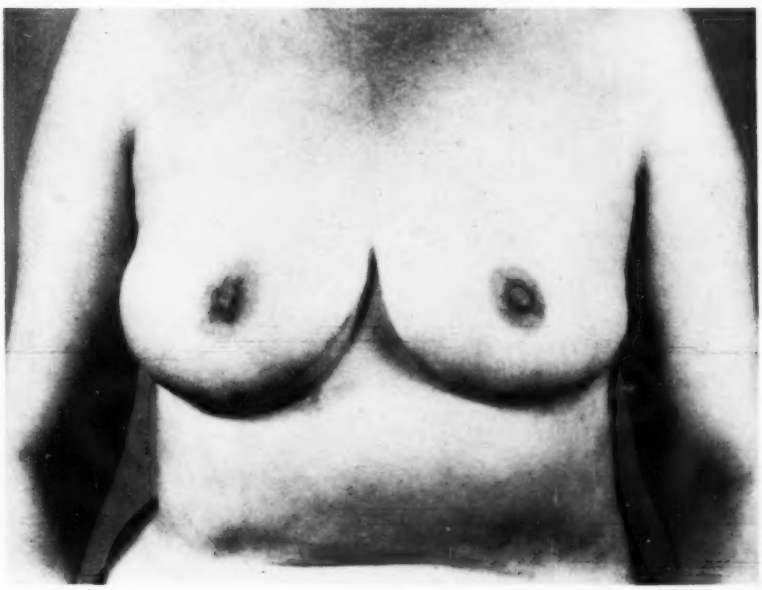
Below
Line of incision for preparation of the graft bed. The basal layer of the skin is conserved in order to provide a rich capillary blood supply for the grafts.

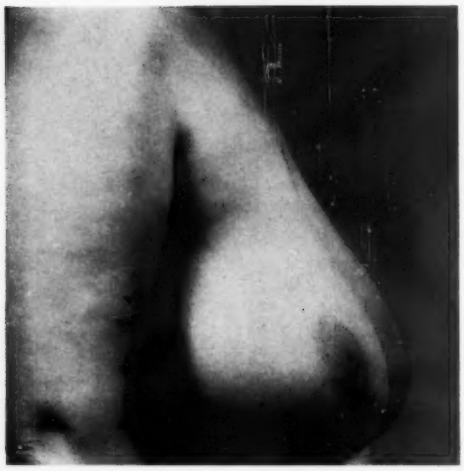




Above
Enlarged pendulous breasts in a woman 44 years of age.

Below
One year after one-stage mammaryplasty with free transplantation of the nipples and areolae.

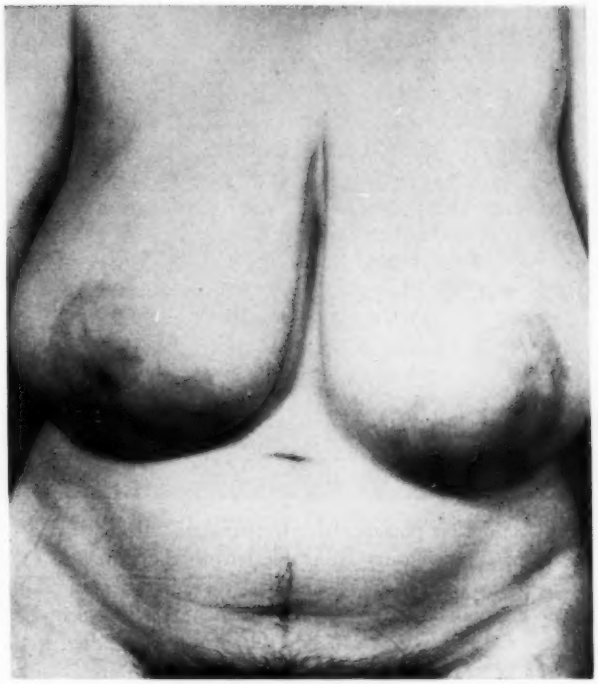




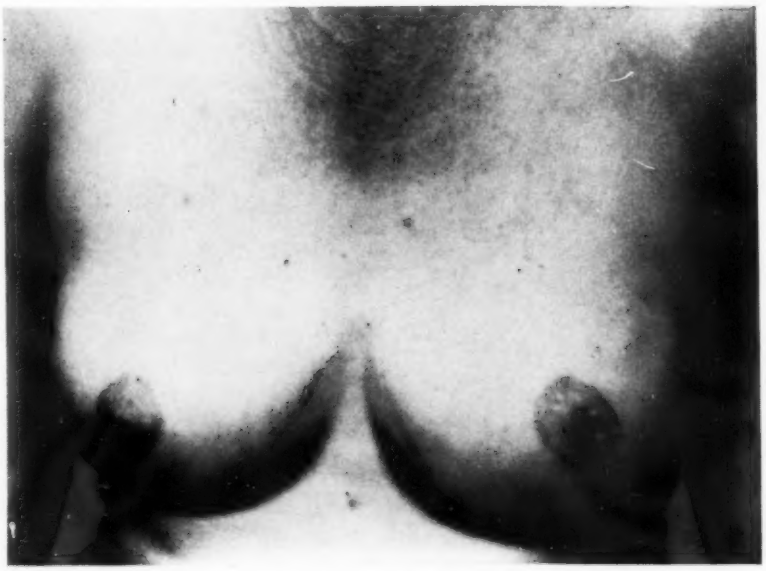
Side view. Preoperative.

Side view. Postoperative.

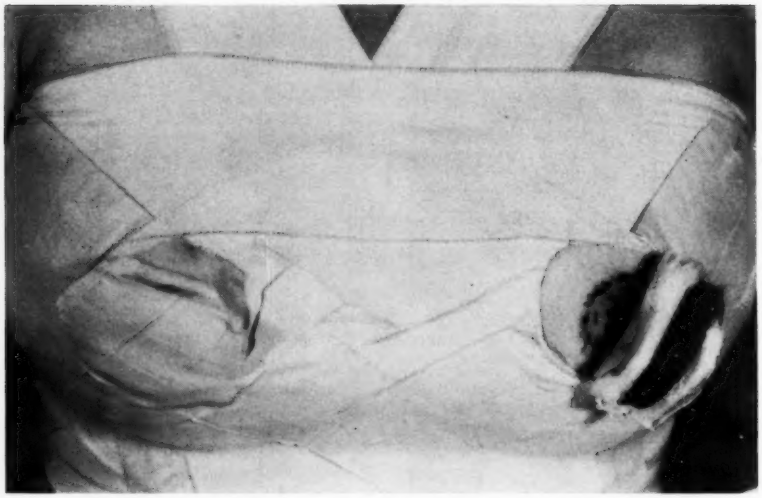
Photograph of the transplanted nipple emphasizing the normal appearance of the nipples and areolae as to texture and form. Without exception all transplanted nipples have had a return of nipple sensation and a return of function of the erectile smooth muscle of the nipple.



Extremely large pendulous breasts extending down below the umbilicus. Patient 40 years of age.



One year after one-stage mammaryplasty with free transplantation of the nipples and areolae.



Window cut in first postoperative dressing on the tenth day to illustrate how the nipple grafts are dressed from the skin out. (1) Layer of vaseline gauze or rayon. (2) About ¼ inch thickness of plain gauze. (3) Layer of rubber sponge ¼ inch in thickness. The central portion of the rubber sponge was "saucerized" to prevent undue pressure on the elevated area. (4) Thin layer of dry gauze. (5) Elastic adhesive.

After complete removal of dressing illustrating the technic of suturing and "quilting" of the nipple grafts.

EDITORIALS

WHAT MAKES BABIES CLICK?

Now that investigators in the field of mental hygiene have focused attention on the early months of life as setting the stage for mental competency or aberration later on, it is becoming more and more important to look into the adjustments of life that a child must make in the early months or even the early weeks.

While it has long been known that a newly-born infant is an automatic individual, acting on a reflex, subcortical level, most physicians have not taken this fact seriously enough to accept its implications in the prescribing of treatment. The analogy between the behavior characteristics of a young infant and a new automobile is closer than one would imagine at first glance. Just as in driving a car we give little thought to the intricate engine purring under its hood, so also do we take for granted and pay little attention to a normal baby's respiratory, cardiac, and autonomic reflexes as they work along so smoothly under the surface. In many important respects the baby clicks entirely on his own.

But just as we realize that the driver has to supply a motor car with the proper oil and fuel and must steer it over the roads, so in many functions of life it is necessary that the baby receive outside help. This is particularly true in his feeding and in his social adjustment to his environment. No matter how efficient he is, no baby can secure his food without assistance and nothing has been built into his makeup to teach him how to react to modern, complicated customs of life. Success in these fields is dependent upon the accomplishment of a co-operative job between mother and baby.

But a baby is not entirely impotent in regard to his feeding. He is equipped with a complicated set of reflexes designed to secure his food if he has a helpful mother. These reflexes are the hunger-appetite-satiety mechanisms, rooting, sucking, swallowing reflexes, and his cry.

The actual neuromuscular reflexes, rooting, sucking and swallowing, are present in all normal, mature babies, but their absence in young prematures makes more artificial methods, such as dropper and gavage feedings, necessary procedures.

Hunger causes pain in the stomach when food is needed and stimulates the hunger cry. Appetite is a psychologic attribute which keeps him feeding until satiety stops the process. These mechanisms are highly automatic and accurate, as any mother knows. Feeding a baby who is under the stimulus of hunger is easy, whereas getting milk into one who is not hungry or whose satiety mechanism has said "No" is almost impossible.

Because the function of feeding requires a co-operative mother, it is essential that she be instructed in how to help. No one would try out a new car without learning how to oil and fuel it. The physician who is familiar with the status of young infants and of their growth potentialities will see to it that a mother learns

to adjust her efforts to those of the baby so that she (1) offers food when his hunger appetite stimulus is active, (2) stops the feeding when satiety shows the red light, and (3) surrounds the feeding situation with as natural a setting as possible, by either nursing him at the breast or holding him close to her during the feeding time. This might be called, from the infant's viewpoint, a "self-regulating regimen." It avoids the inconsistencies of rigid schedules of time and amount of feedings which often lead to undue crying and anorexia. It makes babies click nutritionally.

In directing a child's responses to the many demands of our complex civilization, parents find difficulties in steering the course of the child's progress easily. Here again it is necessary to know the devious but well-marked path of growth and development. The key to success lies in making each new turn at the proper time, when the infant is mature enough to understand it. If we could learn to expect our youngsters to "act their age," many blocks to progress could be avoided. In climbing the rugged road of success in human relationships, we need to adhere closely to its twisting, well-worn path. It will "stall the engine" to go barging off on unfamiliar footpaths up the slopes.

Babies click best when we respect the way they were meant to work, when we "gas up" at the proper times with the right fuel and stick to the well-defined course of normal growth and development.

C. A. A.

CANCER CYTOLOGY

A CONSIDERABLE body of evidence is accumulating which confirms the claim advanced thirty years ago by Papanicolaou, that early cancer can be diagnosed by cytological examination of various body secretions.

In a recent symposium conducted by McDonald and his associates of the Mayo Clinic, this technic was discussed, with particular reference to carcinoma of the lung, urinary tract, and kidney. These investigators found that all the features characteristic of malignant cells, which are seen in sections of tissues, with the exception of invasiveness, could be observed in isolated groups of cells, obtained in a smear.

Sputum or bronchial secretion from 70 patients yielded positive results. In 7 patients the lesions were found in the upper lobe, and were beyond the reach of the bronchoscopist; a specimen for biopsy could not be obtained. Diagnosis, therefore, was established only on the basis of the microscopic examination of sputum or bronchial secretions.

In another 7 patients the bronchoscopic examination was inconclusive or negative. Again, positive diagnosis was established on the basis of smears. Fourteen patients were in such physical condition that bronchoscopy was contraindicated; for this group examination of sputum was simple, quick, inexpensive, and harmless. In 41 cases both the biopsy and smear yielded positive results. There was one false positive; the investigators have pointed out that false positive results occur in about 1 to 3 per cent of examinations, depending in part at least upon the microscopist's experience.

Malignant lesions of the urinary tract were diagnosed by examining microscopically the centrifuged and stained urinary sediment.

The investigators do not suggest that the technic will supplant existing methods of diagnosis, but that it will be a practical and useful adjunct. One of its major uses will be that of "screening" cases of unexplained gross and microscopic hematuria, questionable renal masses, or questionable lesions of the renal pelves or calices as seen in excretory urography. Or, carcinoma of the prostate gland or of the bladder may possibly be diagnosed by this procedure, long before the lesions are observable by current methods.

In applying the Papanicolaou methods to the diagnosis of cancer, an essential prerequisite is that the examiner know cancer cytology. When the pathologist is not only a histologist but also a cytologist, a big step will have been taken in eradicating cancer.

This Month in Medicine

PSYCHOTIC REACTIONS TO QUINACRINE INGESTION

Several authors have reported the occurrence of psychic disturbances following the ingestion of quinacrine (atabrine). The cause of these mental disturbances, however, could not be determined, for the persons taking the drug also had malaria.

Recently, Hoobler has reported severe toxic mental reactions in normal subjects, who had no malaria, and who took the drug for experimental purposes only. Thirty-one medical, dental, and medical administrative officers of a United States Army General Hospital volunteered to take quinacrine in suppressive and then in therapeutic doses.

Large doses of the drug—that is, therapeutic doses—produced mental disturbances in 24 of the 31 officers. The symptoms varied from mild insomnia and depression to severe psychotic reactions, with delusions, hallucinations, and profound changes in mood.

Hoobler suggests that the administration of 0.1 gm. of quinacrine daily for one week, 0.2 gm. daily for one week, and 1.2 and 0.9 gm. on subsequent days approaches the threshold of cerebral toxicity for this drug.

Suggested Reading

Hoobler, S. W.: Psychotic reactions to the ingestion of large doses of quinacrine in normal subjects. Am. J. Trop. Med. 27: 477 (July) 1947.

CHEESE AND DISEASE

Contaminated cheese has caused at least 59 epidemics, 2,904 cases of disease, and 117 deaths in the United States and Canada, since 1883.

Organisms most commonly associated with cheese-borne infections include members of the *Salmonella, Staphylococcus, Brucella,* and *Clostridium* genera. All of these organisms die out quickly at high temperatures. Pasteurization of milk and aging at high temperature, therefore, are the essential means of preventing cheese-borne infections. Indeed, study of the various epidemics has revealed that they have been caused by cheese made from raw milk, which was sold and eaten too soon after it was made.

Many cheese-makers declare that pasteurized milk makes poor cheese. However, critical investigations have revealed that this view is not true, that pasteurized milk makes better flavored and higher scoring cheddar cheese than can be obtained from raw milk. Further, it can be ripened in about half the time, because it can be held at higher temperatures than cheese made from raw milk.

Suggested Reading

Fabian, F. W.: Cheese and its relation to disease. Am. J. Pub. Health. 37: 987 (August) 1947.

Rh IN PATERNITY DISPUTES

Legal precedent was set recently for the use of the Rh factor in settling paternity disputes. The bloods of the three persons concerned in the dispute were found to be compatible, when tested by the usual blood-grouping procedure. The husband could not be excluded as the possible father, on the basis of these tests. The Rh tests, however, revealed that the husband could not be the father, which is what he had contended all along.

The judge accepted the evidence of the experts, and held that the husband was not the father of the child. The remarkable feature of this case is that the judge ruled as he did in spite of the fact that he had no legal precedent by which to be guided. Rather, he established precedent.

Suggested Reading

Current Comment: Rh blood tests in disputed paternity cases. J.A.M.A. 135: 162 (September 20), 1947.

STREPTOMYCIN IN TUBERCULOSIS

STREPTOMYCIN achieves one of its most dramatic effects in the treatment of draining tuberculous sinuses. Recently, Brock has reported the use of this antibiotic in the treatment of 12 patients, of whom 11 were negroes, presenting a total of 60 draining, tuberculous, cutaneous sinuses. Prior to streptomycin therapy, the sinuses had been draining for an average of two years.

The drug was given in daily doses of 1.8 gm., 0.3 gm. every four hours, intramuscularly. Six patients were so treated for ninety days; the remainder were treated for one hundred fifty days, with an interruption of three weeks after the first ninety days.

Ten of the patients had draining sinuses which originated in bone. Some of these sinuses, as well as others, closed within a week or ten days following institution of streptomycin therapy. Within three or four days the purulent material decreased in amount and contained less pus. Induration and tenderness disappeared within a month or so. Bone that had shown radiographic evidence of destruction, gave evidence of regeneration following the therapy.

After beginning streptomycin therapy, 15 per cent of the 60 sinuses closed within one to four weeks, 15 per cent closed within six to eight weeks, 50 per cent closed within ten and twelve weeks, and the remaining 20 per cent closed within thirteen to twenty weeks.

SUGGESTED READING

BROCK, B. L.: Streptomycin in the treatment of draining tuberculous sinuses. J.A.M.A. 135: 147 (September 20), 1947.

PENICILLIN IN PROSTATECTOMY

PENICILLIN used prophylactically, lowers the mortality associated with prostatectomy. This mortality is often the result of infection. Bell, an English investigator, found that by administering 20,000 units of penicillin intramuscularly, every six hours, to all patients with indwelling urethral catheters, the death rate from prostatectomy could be significantly reduced. The penicillin was given routinely, both preoperatively and postoperatively for as long as the catheter remained in place, or (postoperatively) until the temperature returned to normal. Results obtained by Bell in his series of 217 cases attest to the value of this technic.

In Bell's 217 cases of prostatic obstruction, including carcinoma, all treated prophylactically with penicillin, the mortality rate was 3.7 per cent. An earlier series of 508 cases, in the treatment of which no penicillin was employed, had a mortality of 14.1 per cent. Cases of simple prostatic enlargement treated with penicillin gave a mortality of 3.1 per cent; without penicillin, 11.3 per cent.

Before penicillin was available, nearly 37 per cent of all cases of prostatic obstruction were submitted to cystostomy, with a case mortality of 15 per cent. Now, using penicillin, less than 11 per cent require cystostomy, and the mortality is zero.

SUGGESTED READING

BELL, J. G. Y.: Penicillin as an aid in prostatectomy. Lancet, 2:347 (September 6), 1947.

DELAY IN CANCER TREATMENT

COMPARISON of recently accumulated data with those obtained ten years ago, reveals that today the physician is often the one most responsible for delay in diagnosis and treatment of cancer. Ten years ago delay was caused by the patient alone in 44 per cent of cases, by the physician alone in 17 per cent of cases.

During the past decade the public has become better educated to the necessity of getting to the physician quickly, when cancer is suspected. Hence, Leach and Robbins recently reported that today the patient alone is responsible for delay in only 32 per cent of cases, while the physician is responsible in 27.8 per cent of cases. In superficial cancer, such as skin, lip, and tongue cancer, the patient is most responsible for delay; but in cancer of the lung or stomach, the less obvious cases, the physician is the more culpable.

SUGGESTED READING

LEACH, J. W., AND ROBBINS, G. F.: Delay in the diagnosis of cancer. J.A.M.A. 135:5 (September 6), 1947.

R. W. C.

Consultation Service

This special consultation information service is offered as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from members of our Editorial Board best qualified to help. Each question will be answered by mail and those of general interest will be published each month. Address all communications to Consultation Service, *Postgraduate Medicine*, 512 Essex Building, Minneapolis 2, Minnesota.

CHOLESTEROL METABOLISM

QUESTION: Are there any diseases due primarily to disturbed cholesterol metabolism? What are the indications for ordering a blood cholesterol and/or cholesterol ester determination and what are the diseases which cause an elevation or depression of the blood levels? *M.D.—Ohio*

ANSWER: There is insufficient information concerning cholesterol metabolism to permit one to state whether or not any disease is primarily due to this substance. The deposits that occur in xanthomatosis and Schüller-Christian's Disease are rich in cholesterol and its esters. Various people have suggested that a disturbance in cholesterol metabolism may be the cause of atherosclerosis.

The normal serum cholesterol value varies from 120-200 mg. per cent of which approximately 70 per cent is present as the ester. The concentration in the blood may be above normal in the following conditions: primary xanthomatosis, lipoid nephrosis, hypothyroidism, diabetes mellitus, obstruction of the common bile duct, pregnancy, early or mild hepatitis, uremia and in some instances of atherosclerosis.

The blood cholesterol may be less than normal in acute yellow atrophy of the liver and hyperthyroidism. The ratio of cholesterol esters is considered of significance in relation to liver function. Marked loss of parenchymal function is accompanied by a decline in the percentage of cholesterol esters.

VITAMIN K

QUESTION: Should parenteral vitamin K be given routinely to every pregnant woman before labor and to every newborn? What is the proper dosage? *M.D.—Pennsylvania*

ANSWER: There is no use in giving vitamin K routinely to pregnant women before labor because its effect is so transitory. Neither does there seem to be good reason for giving it to every newborn infant because such a small percentage of normal full-time babies show any hemophilic tendencies.

As a routine measure, the only valid occasion for administration of Vitamin K is to all women falling into labor prematurely. The reason for this is that premature infants are more likely than others to develop hemorrhagic tendencies, especially intracranial hemorrhage, and may thus be afforded some degree of protection.

URETHRAL FEVER

QUESTION: What is the present recommended treatment and cause of the so-called urethral fever or urinary fever which comes on after instrumentation of the urethra by passing a sound or catheterization?

In the event a patient has experienced one episode of chills and fever after the passage of a sound, should he be dilated again? Penicillin tablets, 100,000 units, were given after passage of the sound every three hours. The penicillin did not seem to have any effect on the chills.

M.D.—Washington

ANSWER: The cause is thought to be the absorption of toxins and probably bacteria through venous sinuses in the urethra and periurethral tissues. These spaces are opened by dilatation and it is believed that when the patient next voids, the pressure of the urine forces the toxic material into the circulation. There is always some degree of edema after a tight urethra has been dilated. The best treatment is the placing of an inlying catheter

of small size, preferably No. 16 or 18 Fr. This is allowed to remain in the urethra and to drain the bladder for at least forty-eight hours, or until the temperature remains normal, for twenty-four hours. Penicillin is administered; sulfathiazole sometimes is administered coincidentally.

USE OF POTASSIUM THIOCYANATE IN HYPERTENSION

QUESTION: I have observed that four or five patients I have treated with potassium thiocyanate for hypertension have developed either tachycardia or frequent extrasystoles, with good results in lowering their blood pressure. I have not used excessive dosage but have tried to maintain their blood level between 8 and 12 mg. per 100 cc. Could you tell me if other doctors have observed this effect of thiocyanate or whether it is any contraindication to its usage? *M.D.—Ohio*

ANSWER: Considerable experience with the use of potassium thiocyanate in essential hypertension has failed to indicate that either extrasystole or tachycardia is a common complication. Unless either of these is marked, it would seem to be no contraindication to the continued use of potassium thiocyanate, inasmuch as there has been favorable reduction of blood pressure.

TREATMENT OF LUES

QUESTION: A white male, 31 years of age, has been under treatment for lues for approximately one year.

When first seen this patient already had secondary lesions, and his serology was strongly positive. He was given a course of pencillin in beeswax and oil consisting of one daily injection for twenty days. However, this afforded no demonstrable benefit. He was then given semi-intensive therapy consisting of 40 injections of Mapharsen (0.06 gm.) and 16 injections of bismuth subsalicylate (0.2 gm.) in twenty-six weeks. At the end of this course, the patient had a negative Kolmer and a strongly positive Mazzini. (Quantitative Mazzini was 41000-0). One month later the Kolmer was moderately positive and at the present time both Kolmer and Mazzini are strongly positive (Quantitative Mazzini is 444 32-0). There are no luetic lesions or clinical signs evident at this time.

What further therapy is now recommended? *M.D.—Pennsylvania*

ANSWER: Results from the use of penicillin in beeswax and oil for patients with early syphilis have not been so satisfactory as those from the intramuscular use of penicillin given at three-hour intervals for a total of approximately 4,000,000 units. The successful results from the beeswax-oil combination are approximating 65 per cent.

Before further treatment for the patient described is outlined, it would be advisable to examine the patient's cerebrospinal fluid, because it might well be that the relapse of results of serologic tests of the blood are due to the fact that the patient has a positive cerebrospinal fluid. If the fluid is normal, it would seem advisable to give the patient a third course, consisting of penicillin administered at the rate of 50,000 units every two hours for a total of 80 injections, which course, if need be, can be repeated in two or three months. On the other hand, if the cerebrospinal fluid is found to be positive, it would be necessary to know the degree of positivity of the fluid before it could be determined whether or not the patient is a candidate for fever therapy.

Book of the Month— A Report

SURGERY OF THE AMBULATORY PATIENT*

DRAWING upon his experience at the University of Pennsylvania Hospital outpatient department, Dr. L. Kraeer Ferguson presents a very comprehensive and informative compilation of ambulatory surgery. The value of this book is evidenced by the fact that it is the second edition of a rather recent publication. The author includes in this edition the new therapy of penicillin and sulfa drugs in surgical lesions.

There are many advantages to ambulatory surgery: it is advantageous to the hospital because it reserves the beds for patients actually needing bed and nursing care; according to Ferguson, fewer complications develop after operations on ambulatory patients than after similar operations performed on hospitalized patients. For example, in a large number of anal operations on ambulatory patients, retention of urine has never been encountered as a complication although this is well known as a frequent and troublesome complaint of the hospitalized patient. It must be understood, however, that the selection of patients is of major importance. When diagnosis is doubtful or when extent of the lesion is not definitely known, the operation should not be performed on the ambulatory patient at all.

The preparation for, and the conduct of, operations on ambulatory patients and postoperative care are discussed in two separate chapters. The chapter on dressings and bandages is unique because of Dr. Ferguson's ingenious application of simplified dressings and use of adhesive. Methods for applying non-cumbersome dressings that will hold over a long period of time are excellently illustrated in pen and ink drawings. The young practitioner will greatly appreciate the extremity dressings that are shown because of their simplicity of application, and precision and neatness of appearance.

Local anesthesia is preferred by the author, with procaine hydrochloride being judged the most efficient local anesthetic agent which has survived the test of extensive clinical trial. It has been the anesthetic agent of choice in 87 per cent of the operations in Ferguson's surgical outpatient clinic. A drug which he has found successful for local anesthesia in the opening of superficial abscesses is pure phenol. Excellent illustrations for the technics of local anesthesia are shown.

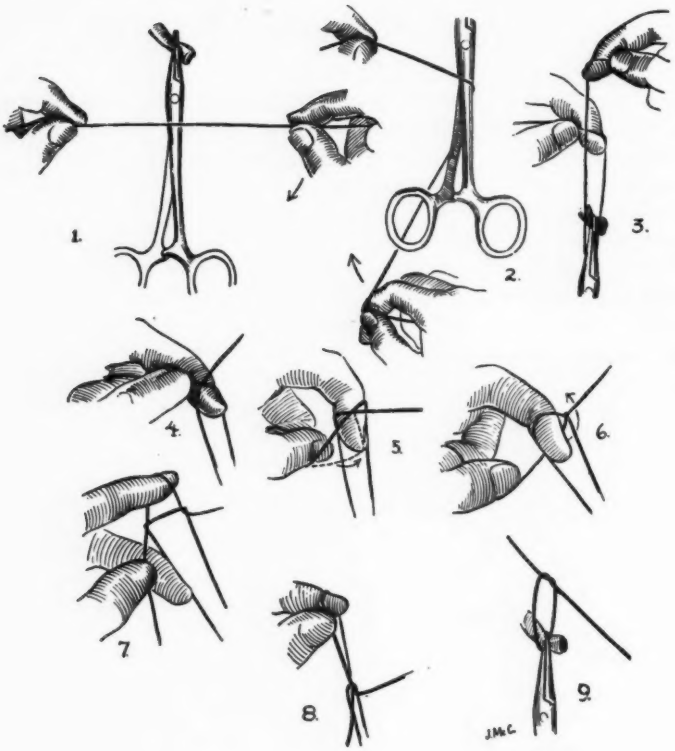
Treatment of inflammation due to infection is discussed with a physiopathologic approach. A review of the mechanism of inflammation introduces the chapter. The local application of external heat, elevation of the area of inflammation, physiologic rest through immobilization, and incision and drainage when suppuration is present are the fundamental principles for treatment of infection. Some physicians may place more emphasis on one of the foregoing tenets than the others, but, in general, if the procedures outlined are followed success is assured.

The mode of use and therapeutic action of the sulfonamides is included in the section on chemotherapy in the treatment of infection. Dr. Ferguson correctly emphasizes the great caution needed in the administration of sulfonamides to the ambulatory patient.

The use of penicillin in peanut oil and beeswax mixtures, both orally and locally, is advocated for the ambulatory patient because the intravenous and round-the-clock intramuscular injections of penicillin are avoided. A newer antibiotic, tyrothricin, is suggested as a topical application for the treatment of wounds and ulcers that are infected with pyogenic cocci.

There are separate sections devoted to the etiology, symptomatology, and treatment of lymphangi-

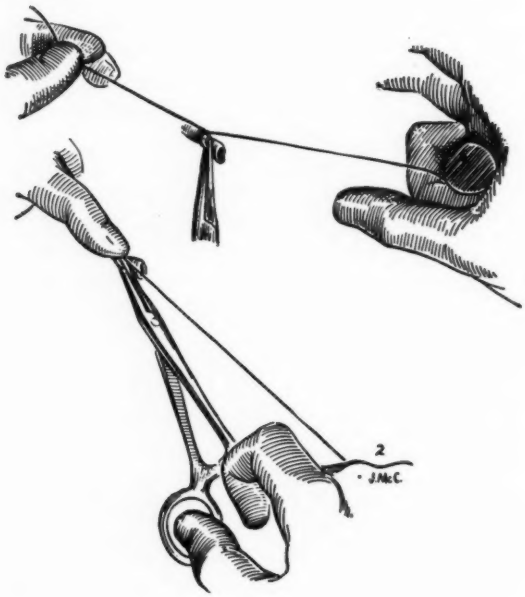
*Surgery of the Ambulatory Patient. By L. Kraeer Ferguson, M. D., with a Section on Fractures by Louis Kaplan, M. D. 901 pages, 645 illustrations. 2nd Edition. J. B. Lippincott Company, Philadelphia, 1947. Price $10.00.



Method of Ligating Vessels Without Assistance

The ligature is held in the right palm. The free end of the ligature is grasped between the left thumb and index finger. The ligature is carried underneath the hemostat with the right hand and a finger tie is then made with the left thumb and index finger and pulled tight.

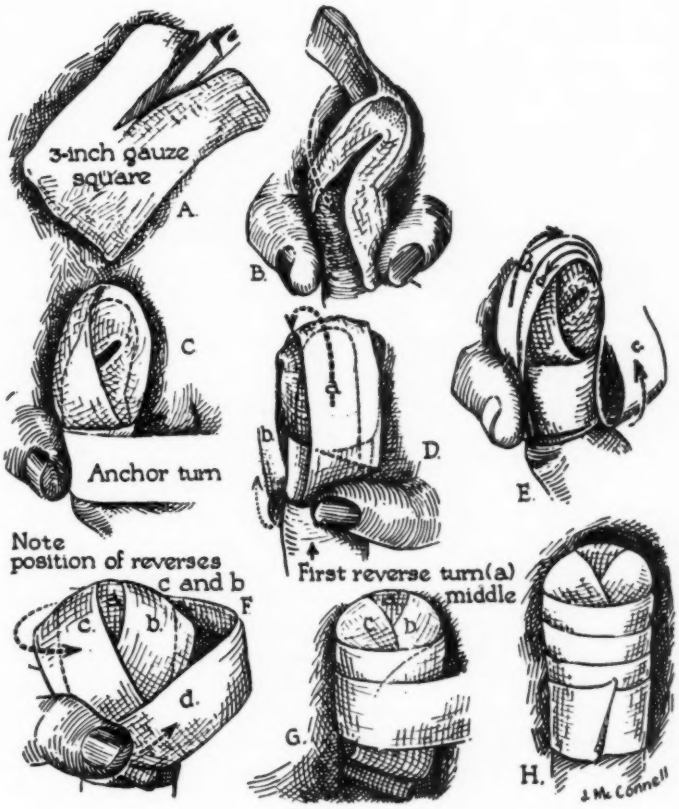
Maintaining the tension on the ligature spool in the right palm, and with the left forefinger holding the tie snugly in place, the hemostat is freed with the right thumb and index finger. A second tie is then made in the same manner.



Illustrations from Ferguson: Surgery of the Ambulatory Patient.

Dressing for the Finger

For dressings of the finger tip following an incision and drainage of an infection of the distal closed space, the 3-in. sterile gauze compress is cut as shown. The loose ends are then folded over the finger tip and the dressing is completed with circular turns about the gauze and recurrent turns over the tip of the finger.



Method of Applying a Dressing to the Foot

Bandages to the ankle and foot are most conveniently applied in figure-of eight turns around the foot and ankle. Two-inch bandage is usually used, with fixation by half-inch adhesive.

tis, cellulitis, erysipelas, erysipeloid of Rosenbach, acute lymphadenitis, dermatitis repens, meleney ulcer, tetanus, anthrax, human, animal, snake, and insect bites.

A comprehensive discussion of the treatment of burns and frost bites is included, and many useful surgical technics are described in a chapter on foreign bodies, superficial cysts, and tumors.

Part Two of the book, devoted to Regional Surgery, consists of thirteen chapters on the more specific lesions of the various parts. It begins with lesions of the scalp and progresses anatomically downward to the toes. One must admire the courage of the author in performing the type of operations he has done on ambulatory patients. With as much experience as Dr. Ferguson has, it is probable that they can be done, but for the novice, such things as elevation of a depressed fracture of the zygoma preferably would be done in a hospital. It must be understood that there is a difference between an out-patient who is ambulatory and a hospital patient who is ambulatory. Therefore, it may be that some of the advised procedures are done on patients who are in a hospital but are still ambulatory.

The information given in the section devoted to the peri-anal region, anus, and anal canal will more than suffice for the average physician's needs for knowledge and practical technics for lesions in those areas. Dr. Ferguson has justifiably exercised great care in writing this chapter because lesions of this area when not treated correctly for itching and pain can result in great distress. The illustrations are more than adequate even for the physician inexperienced in proctology.

The genitourinary tract chapter includes some of the more recent treatments found successful in the Army. The ambulatory treatment of gonorrhea in the male with penicillin is given and Dr. Ferguson suggests that in cases when penicillin is ineffective, a combination of both penicillin and a sulfamide has been found successful.

The third and final section of the book was written by Dr. Louis Kaplan and is devoted to fractures. It is introduced by general considerations of etiology, pathology, diagnosis, and principles of fracture treatment. The author then discusses most of the fractures commonly handled in general surgical practice. The discussion is well organized and extensive and should prove useful even to an orthopedic surgeon. The illustrations and roentgenograms are typical and are good reproductions.

The book should be of great value to the medical student, recent graduate and general practitioner. It is encyclopedic in its content and all references are listed in bibliographies at the end of each chapter. One must understand, however, that the simplicity of presentation of technical procedures may belie their practical value, for a thorough knowledge of surgical principles and keen surgical judgment is still a must for a physician using the book for reference.

RECEIVED THIS MONTH

OCULAR THERAPEUTICS, by William J. Harrison, M.D., Associate Professor of Ophthalmology, Jefferson Medical College; Chief of Ophthalmological Clinic, Jefferson Hospital; Attending Surgeon, Wills Hospital, Philadelphia. This pocket manual deals with the various drugs whose ocular therapeutic values have been determined by extensive clinical use. Charles C Thomas, Publisher, Springfield, Ill., 1947. Price $3.50.

TRICHOMONAS VAGINALS AND TRICHOMONIASIS, by Ray E. Trussell, M.D., Associate in Hygiene and Preventive Medicine, State University of Iowa. With an introduction by E. D. Plass, M.D., Professor of Obstetrics and Gynecology, State University of Iowa. A bibliography of 1586 references is included, along with 19 figures and 16 tables. Charles C Thomas, Publisher, Springfield, Ill., 1947. Price $6.00.

MEN OF MEDICINE

THE GENERAL ASSUMES COMMAND

In the handsome oak-panelled corner office on the seventh floor of the American Medical Association building in Chicago, sits a broad-shouldered, genial man who is the new Secretary and General Manager of the Association. He well becomes the office, and its duties present no hazards of flank attack or ambush for an old army man with thirty-three years of service with its Medical Corps to his credit. When he resigned from the Army in 1945, George Fairless Lull was Deputy Surgeon General with the rank of Major General. A.M.A. headquarters refer to him proudly as "The General" and more than one little typist as she watches the tall soldierly figure stride down the hall has been overheard sighing, "Wouldn't it be wonderful if he still wore his uniform!"

He first donned the army uniform in 1912, apparently motivated by youthful bravado and sheer stubbornness, but the gratifying regularity of his advancement in rank demonstrated that his decision was soundly based on innate aptitudes. The ingeniously administered advice of a wise teacher was important too.

George Lull, born in Scranton, Pennsylvania, received his M.D. degree at Jefferson Medical College in 1909, then interned at Jefferson Hospital. In 1911, bearing the lugubrious title of Demonstrator in Morbid Anatomy, he handled autopsies for Philadelphia General Hospital and was assistant to Dr. W. M. L. Copeland, an excellent pathologist, a hard taskmaster, and—as appeared later—a psychologist of unusual discernment.

"How I happened to enlist was really odd." Dr. Lull's smile deepened as he reflected on the irony of that choice. "There were several of us youngsters working at Jefferson, and one week end with permission to go to Baltimore, three of us ended up visiting with some of the army boys in Washington. I was interested in the experiments they were doing with inoculation for typhoid and typhus. When we got back, the first thing I knew Copeland yanked me in and announced that if I was fooling around with some notion of going into the army, I might as well understand at once that he had no intention of renewing my contract! I needn't think I could flunk the exams and then flop back onto Jefferson. Well, I was flabbergasted. I'd had not the slightest intention of trying out for the army until he made that speech. But it got me sore and I decided I'd show Copeland I could get into the army if I wanted to. I knew it would be tough—only 5 per cent of the applicants were being accepted—but I took the exams that fall along with fourteen others. Only three of us made the grade and went on to the Army Medical College in Washington. Copeland was rather stiff and formal when I said good-by. Never saw him again till 1919 when I ran into him in Germany and we had dinner together. He told me then he'd known from the beginning that I'd make a good army man, but I was so darned bull-headed he knew it was no use suggesting it as a career. So he played it the other way, got me so mad that I went in to prove to him I could."

Dr. Copeland, at long last, was thus proved as a vocational diagnostician as well as pathologist. He had recognized Lull's interest in clinical pathology and his indifference to making money. And most certainly the army proved to be the right place for young Lull. It provided him with varied opportunities and enabled him to develop surprisingly diverse talents.

On his first tour of duty outside of the United States Dr. Lull served as medical officer for the 29th infantry in the deserted ghost town of Culebra in the Panama Canal Zone. One battalion was sent to act as lock guard at a new post: Gatun. There he learned how a native of a malaria-infested country acknowledges his daily two tablets

of quinine prescribed by the army: He turns his tin cup upside down to prove that he's drunk the water; he says clearly "Thank you," not to conform to etiquette but to demonstrate he's not concealing the tablets under his tongue!

Before his tour of duty in Panama was completed, Dr. Lull was brought back to McAllen, Texas to build a camp hospital for the National Guard then stationed on the Mexican border. Squadron A was made up of light-hearted New York youngsters who'd joined up to ride the horses provided at the National Guard Armory and to have fun generally. Dr. Lull remembers them affectionately when he says:

"I needed to staff a laboratory at the hospital and when I interviewed the three men they sent over I found they were all young doctors. Best staffed laboratory I ever saw. Every man in the squadron became an officer and later they were all in France. Made fine records, too."

There were more training camps to lay out and camp hospitals to build before Dr. Lull managed his own transfer to France. One of the largest was the two thousand bed hospital at Camp Beauregard, Louisiana. "And do you know what most of the patients in those beds were suffering from? Measles and mumps! The boys were recruited chiefly from country districts in Louisiana and Mississippi. They'd never been exposed to such diseases enough to build up any immunity, and childhood plagues ran through that place like wildfire."

George Lull, chafing at orders that kept him in Louisiana when he wanted to be in France, patiently filled in the War Department questionnaires inquiring what available officer could accept full charge of the hospital. With monotonous regularity, he wrote down the name of Major John T. Burrus. At last came a telegram from the War Department reiterating the question already asked innumerable times. Dr. Lull wired Major Burrus' name to Washington. A cautious telegraphed inquiry from the War Department was his reply: "Will you, George F. Lull, assume full responsibility for all Major Burrus' actions in your absence."

Recklessly, Dr. Lull sent off an unconditional yes, proceeded to France and took over the command of base hospital Number 35, sponsored and completely staffed by the Good Samaritan Hospital of Los Angeles. For faithfulness and distinction in discharge of his duties, he was awarded the Certificate of Meritorious Service by General Pershing, a decoration reserved for a very few outstanding individuals. Years later all the men who had been recipients of so high an honor were also given the Purple Heart, so that accounts for another of the General's impressive row of ribbons.

In WORLD WAR II, Dr. Lull, then in his late fifties, served the entire time, as he ruefully observes, in the Army of the Potomac with headquarters in a commandeered apartment house. He was in charge of personnel, a position for which his abilities and kindly human warmth made him particularly suitable. Speaking appreciatively of his fellow doctors, he says:

"The medical profession of the United States can take great pride in the fact that through a purely volunteer system its members offered their services in such large numbers. Many men who had to remain at home in essential positions were bitterly disappointed that they could not participate as members of the armed forces.

"It would not be just to close . . . without mentioning the doctors in the older age groups who volunteered in such large numbers. Many of them who were sixty years of age traveled long distances to Washington to plead that they be given a chance to enter the Army. They, as well as their fellows in the service, can be proud of their profession's war record."

When Major General Norman T. Kirk was appointed Surgeon General of the Army, George Lull was made a major general, and given the position of Deputy Surgeon General. Among his new duties was the supervision of the recording of innumerable statistical tables, a task that presented few difficulties to a man who had originated the course in Vital Statistics in the Army Medical College.

Dr. Lull also likes to recall his years of duty as medical adviser to the Governor-General of the Philippines. He served in that capacity under three different men: Theodore Roosevelt, Henry L. Stimson, and Dwight F. Davis. It was with Davis that

GEORGE F. LULL, M.D.

Dr. Lull was most closely associated and with whom he undertook a five hundred mile informal inspection trip of Mindanao. Dr. Lull refuses to dramatize the experience, stating flatly that their expedition was not through the country of the headhunters.

On this trek the two men were accompanied by Davis' young son, Pete, an Army captain, an aide, and an interpreter who understood the differences between such closely related dialects as Malano and Bagobo!

"That interpreter was a clever fellow," reminisces Dr. Lull. "He lived permanently in the Islands; incidentally, I heard not long ago that he was captured and tortured to death by the Japanese."

In those days, when the little party of five men waded upstream, rode in dug-outs when they could, camped where they found themselves, or were occasionally lucky enough to find accommodations in one of the small schoolhouses that were a landmark of the American occupation, the natives were curious but generally friendly.

At a ceremonial council meeting, one chieftain diplomatically announced that he welcomed American rule for himself and his people, but he would have none of those despised Visayans who merely aped their betters. His tirade was directed against the Filipino Christians generally, although the term Visayan that he used with such contempt, applies properly to a large group who, with the better known Tagalogs, constitute the majority of civilized Filipinos. Another remote tribal leader,

less polished but more frank in his expression, made a long speech apparently of incredulity and amazement. The interpreter translated freely: "He says he's heard of God and of the Governor General, but he'd never expected to meet either of them in person!"

Dr. Lull points out that few people realize the great extent of the Philippines—actually the Islands extend from north to south a distance as great as that from Canada to the Mexican border. Moreover, eleven of the islands have an area of more than a thousand square miles apiece, and the terrain varies from malaria-infested swamps to inaccessible mountain peaks.

Being entrusted with the health of so widespread a population was a tremendous responsibility. The mixed racial origins and religious beliefs of the people complicated matters still further. One example is typical: The Mohammedans—of whom there are some 500,000 in the Islands—would not allow themselves to be touched by Christians. Since the Army medical officers and most of the trained native assistants were Christians (probably recruited from the able Visayans and Tagalogs of Luzon), this tabu meant that Mohammedan groups were constantly neglecting routine immunization and inoculation. Other factors were the reluctance of the fledgling Filipino legislature to appropriate sufficient funds for public health, and the occasional native carelessness in handling serum or neglecting to provide new seed stock. The American policy of keeping hands off and letting the Filipinos learn by experience made the task still more delicate.

In spite of setbacks and obstacles, a remarkably fine public health program was set up and maintained in the Philippine Islands, and Dr. Lull was one of the men who made possible the success of that program.

After his return from France in 1919, Dr. Lull had been sent to organize the First Corps Area Laboratories at Fort Banks, Massachusetts. By then he had added to his original bent toward pathology, an active interest in sanitary engineering and preventive medicine. Taking advantage of being stationed near Boston he attended seminars at Harvard. The school itself was set up under the auspices of Massachusetts Institute of Technology, Harvard Medical School, and the School of Sanitary Engineering of Harvard University.

Sedgewick of M.I.T., Professor Whipple and Dr. Rosenau of Harvard combined their efforts to make the courses unusually valuable. Upon completion of the work there, Dr. Lull received his certificate in Public Health. Several years later, on an eight months' leave of absence from the Army, he completed his academic training at the University of Pennsylvania, receiving the degree of Doctor of Public Health.

In 1929 he returned to the Army Medical School in Washington where, during the absence of Henry Nichols he acted as head of the Department of Preventive Medicine, remaining as assistant head for three years after Nichols' return. He was responsible for adding to the curriculum new courses in Vital Statistics and Sanitary Engineering.

Sympathetic insight and warm human understanding do not ordinarily distinguish Army administrators, yet exactly those traits characterize George Lull. Among his army colleagues and the men who worked under him he was dubbed, with trust and respect, a square-shooter. Operating in the miasma of professional jealousies and thicket of red tape that hedge Army procedure it's not easy to continue to deserve that forthright epithet.

The "General's" geniality is neither a mood nor a front, but goes all the way round and all the way down. A constantly functioning sense of humor is one of its components. Thus Dr. Lull can relate with amusement of the time the Army ordered him to proceed from Fort Sam Houston, Texas, to San Francisco en route to the Philippines via Nicaragua and New York aboard a transport vessel rather than pay railroad fare from Texas to California! The ship ran aground and put into the Canal Zone for over a month, but that delay, too, he not only took in his stride but utilized. A throw-back, he conjectures, to the calm and solid sense of a remote ancestress of his in Byfield, Massachusetts who, when she was only five, was captured by the Indians not many years after the first Lull had settled in Ipswich in 1670. The little girl was never seen again by her family nor by white people until she emerged from the forests some sixty years later,

tough, leathery, unregenerate, and utterly bored by the idea of resuming the effete and finicky ways of the English settlers!

In his steady rise to eminence Dr. Lull has avoided conflict and useless kicking against the pricks. During the war, in his position as director of personnel, he saw the unending friction between army regulations and the rebelliousness of individual practitioners. It is a tribute to his nature that while understanding the natural opposition, he himself has never found occasion to resent discipline nor has he ever had to accept arbitrary professional dictation from a line officer.

Possessed of such a notable degree of sympathetic understanding, Dr. Lull nevertheless chose the broader applications of medicine rather than the confines of laboratory research or the intimacy of doctor and patient. Yet in his early childhood it was a country doctor of the horse and buggy era that first excited his deep admiration, and kindled in his heart a desire to be like him. To young George, the child of prosperous but simple farming people, old Dr. Paine represented hope in time of trouble, relief from suffering, reprieve from the fear of death itself. All those emotions struggled inarticulately below the surface of the boy's consciousness as he watched the familiar figure on the roads of the community in all seasons, all extremes of weather. Once it was George's own brother who lay feverish and gasping in distress, though the scarlet fever which the family had recognized and treated should have long been over. It was dark and windy and very late at night when the faithful Dr. Paine arrived, but he brought with him a blessed sense of security and freedom from the fear that the child who had waited so anxiously never forgot.

Probably from that early admiration stemmed George's determination to become a doctor, for there were none in his immediate family background. There are now, however, for not only did George Lull become a doctor, but so did his brother, and his brother's son, and his own son. Thus he stands at the beginning of a dynasty, for his son has followed in his father's footsteps by enlisting in the Army Medical Corps and is stationed at Fort Sam Houston where his father once served. But time—and medical progress—accelerate with dizzying speed. The son's specialty is not hospital engineering or sanitation but radiology.

As a spokesman for the A.M.A., Dr. Lull speaks out clearly his praise of the family doctor who understood the patient's background, disposition, circumstances as well as his ailment—who indeed practiced psychosomatic medicine without knowing it. As he is fond of putting it, "We must treat the patient rather than the disease." And he sees an ever-broadening field for the general practitioner even in these days of highly differentiated specialization. . . . "There is a great need for qualified general practitioners of medicine, in many more areas, relatively speaking, than there is for specialists. Many areas fully able to support a few general practitioners are unable to support specialists but, as more and more young men elect to take specialty training, fewer will be available to perform the duties of general practitioners. I have no solution for this problem, but I know it is of interest as it is closely related to the distribution of medical care and to the training of physicians."

To his present job as Secretary and General Manager of the A.M.A., Dr. Lull brings broad resources of medical knowledge and ability to deal with medical personnel. Nor is he a stranger to A.M.A. procedure. For three years he served as the Army delegate to the House of Delegates of the A.M.A. During the war in his position as Deputy Surgeon General, he was constantly in touch with the activities of the A.M.A. in classifying, contacting, recruiting, and assigning doctors to the military services and our home population.

Now the A.M.A. under the able leadership of its proved and war-tested general has resumed its peacetime activities. Some of its earlier campaigns have achieved such success that they are long since chalked up as milestones in medical history. For example, rigid and uniform requirements in medical training was an objective toward which the Association struggled for years. Dr. Lull speaks of the present situation: "It is only in the last fifty years that this big improvement in medical education has taken place. Now we have only one school operating in the United States that has not been approved fully by the A.M.A. There are one

or two others on probation, they haven't been fully approved, but the A.M.A. now is the referee, so to speak, of whether or not the student is receiving the proper type of medical education. All of us who have lived during the early years of this century realize that it has taken a great many years to establish this basis, and to set up standards that could be enforced in medical education. We now look with satisfaction upon the fact that we lead the world in medical education."

Similar uniform standards have been set up and enforced in regard to hospitals.

An interesting shift of emphasis has occurred in the department that once investigated and tried to get rid of patent medicines and quackery. Today its quarters and its personnel have, because the job was so well done, shrunk to comparative insignificance. On the contrary the drug houses and pharmaceutical firms, once wary and suspicious—sometimes even actively hostile—now clamor to have their products tested and blessed with the A.M.A. stamp of approval. As a consequence the physical and chemical testing laboratories have grown apace, spreading over a large part of one floor, and employing highly skilled experts in both fields.

As a matter of fact the whole eight floors of the dignified but modern building on North Dearborn abound with experts. Some retire to a quiet corner and read, translate, edit, and abstract material from the leading medical journals of France, Spain, Sweden, Russia and Czecho-Slovakia. Necessarily, linguists who are also doctors are at a premium. They get on nicely with their neighbors, the library staff. A special contingent provides reference material for physicians, sending out so-called "package libraries" to a man worried over a puzzling case that defies his diagnosis with a parade of contradictory symptoms, or assembling material for a hard-pressed doctor with a speech to the county society looming ahead of him. Like other of the branches requiring skilled and experienced workers, this service is badly understaffed, a condition that seriously cuts down its usefulness.

Finding competent, trained personnel has been another problem for Dr. Lull. Resourcefully he added to the skilled clerical staff by employing veterans part time while they're attending college in Chicago. But sometimes he must wish he could merely requisition from the inexhaustible man power supply once available to the army, two Russian translators, six laboratory assistants, ten librarians, a motion picture operator, and a score each of experienced clerks and typists!

The movie projection man would come into his own in a diminutive specially built room where films illustrating new surgical technics or the crystallization process of a new drug can be run off at any moment. Many of these films also are available for county or state medical groups. And as Dr. Lull colloquially terms them, platters too are available for medical groups—thirteen series of them on as many different topics, sufficient to keep a medical society broadcasting once a week for four years. There are also graphs and charts and maps and posters, making vividly concrete such diverse problems as the incidence of typhus over the world, and the best places in the United States for a young doctor recently released from the army to hang out his sign.

Tucked away in another corner is the ethics department, which is acutely aware that such new technics of education as the film and the radio present their own confusing issues. Here again the trend has changed from suppressing and forbidding to persuading and urging ahead in legitimate channels. "Believe it or not, sometimes we practically have to beat our own colleagues over the head to make them see that telling about the new operation they've discovered over the air may be the finest thing in the world for the medical profession. If it's done under the auspices of the A.M.A., that is, and not as a private promotion scheme of some radio station or sponsor."

Dr. Lull is especially proud of the program "Doctors Then and Now" that ran for twenty-six weeks on N.B.C. and received the first award for public service programs from the Eleventh Institute for Radio in Education of Ohio State University. The N.B.C. show is only one of several, for programs were broadcast in 1947 on all four major networks.

A.M.A. encouragement of voluntary plans for health insurance is whole-hearted. Indeed the Association practices what it preaches to such a degree that there is no corridor or restroom without its warning notice urging employees to report any

injury at once. For general circulation it has published a reliable directory of plans containing detailed and comparable data on each, and has also devised a set of standards for use as a guide in issuing the seal of acceptance. And when the A.M.A. assembles data and files it, as they have done on their complete roster of physicians in the U.S.A., the F.B.I. had better look to its laurels! What isn't in the A.M.A. cards not even the doctor's best friend could tell you. Just in passing it might be well to warn John L. Lewis that the Council on Medical Service has undertaken a special study and follow-up of the United Mine Workers' Health fund!

The Council on Industrial Health gives another instance of how the A.M.A., instead of limiting itself to discussions of clinical medicine and surgery, has extended broadly into the related fields of medical economics, public relations (there's a whole department) and social legislation. The Council studies such specific matters as rehabilitation and employment of the handicapped, air conditioning and ventilation, noise control, women in industry, mental and personal hygiene of the worker. The list might easily be made even more imposing, but Dr. Lull feels that in that particular field the most notable gain has been professional acceptance. As he sums it up: "More and more physicians are realizing that in industrial health there are great possibilities for professional advancement as administrators, consulting specialists, clinicians, and investigators."

But despite the multiplicity of bureaus, councils, and committees the general manager can spare a thought for the problems of the seven hundred or more workers currently employed by the A.M.A. Under his regime there has been set up the Bureau of Industrial and Personnel Relations. Not only has every job at Association headquarters been carefully evaluated, but a sincere attempt is being made to keep everybody happy by promoting and transferring individuals from one department to another when a vacancy occurs rather than to have each office act as a separate unit.

Even so hit or miss a sampling of the various activities constantly advancing under the aegis of the A.M.A. and the watchful eye of Dr. Lull gives some idea of their diversity and scope. A light rein and an easy hand characterize Dr. Lull's method of helping everyone to pull together and to pull ahead.

"Routine matters slide along easily enough, and even some not so routine," smiles Dr. Lull. "And I like my job of liaison between our members and the Association, telling them what the Association has to offer them. Not a bad idea to let them know how they can help the Association either. Nothing I'd like better than lots of letters with questions, suggestions, yes, even gripes, from the doctors." His hazel eyes regarded the glass-topped desk speculatively, and suddenly the quiet smile deepened into a chuckle. "Not that I ever want to be confused with a contest judge or a music publisher again! You know I was once. Speech I made during the war, and I happened to mention that it was too bad no good marches had turned up in this war. There were plenty of 'em last time, but nothing now except a couple of sentimental ballads like 'The White Cliffs of Dover' or 'Lilli Marlene'—and that wasn't even ours. We didn't turn up a 'Pack Up Your Troubles in Your Old Kit Bag' or even a 'K, K, Katy.' Anyhow that remark I just happened to make was the only thing the A.P. men quoted in the papers, and in less than a week my desk was literally buried in marching songs sent in from everywhere! Some of 'em had just the music and wanted me to write the words, some of 'em sent in words they wanted me to refer to Irving Berlin for a tune! It got to be the joke of the department. Songs, music, lyrics—hundreds, thousands of 'em. Must have thought I was Sousa!

"Oh, I appreciate mail, lots of it; but no more music clearing houses."

Rather a predicament for a busy Deputy Surgeon General, but perhaps he might contribute to the A.M.A. in addition to his more conventional duties, a really rousing good song, something reminiscent of marching men in far-flung lands, men defying, attacking, conquering the worst enemies of all, ignorance and pain and disease. Dr. Lull is an old campaigner in that unceasing battle and his encouraging voice is one that his fellow soldiers like very much to hear.

L. C. DEINARD

1947 Prize Winners in American Physicians Art Association

Exhibited at the Centennial Session of the American Medical Association, Atlantic City, June 9-13.

1. "The Cow Barn," pen and ink. Solomon Fineman, M.D., New York, N. Y.

2. "Lusk's Point, New Zealand," Kodachrome. L. Allan Erskine, M.D., Palmerton, Pa.

3. "Portrait, Dr. H. S. Appell," oil. J. Louis Jack, M.D., New Haven, Conn.

4. "Miniature Bed," woodwork. David Rose, M.D., Belmont, Mass.

5. "Spring House," linoleum block. A. R. Pittman, M.D., Trenton, N. J.

6. "William Ryan," plaster. Helen Ryan, M.D., Philadelphia, Pa.

7. "Portrait of Mother," oil. John F. Smith, M.D., Los Angeles, Calif.

8. "Interior (of an interior)," drawing. Beatrice Raymond, M.D., Chicago, Ill.

9. "Battle Winner," bronze. Edward G. Deming, M.D., West Hartford, Conn.

10. "Franklin D. Roosevelt," sculpture. Harry Weiner, M.D., Brooklyn, N. Y.

11. "Rose Bouquet Afghan," needlework. Clare N. Reese, M.D., Oraville, Calif.

12. "Autumn Flowers," watercolor. A. C. Isham, M.D., Pittsburgh, Pa.

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What Other Editors Think

Editorial Evaluation of Current Contributions To Medical Progress

MEDICAL GENETICS

THE recent observance of the 100th anniversary of the New York Academy of Medicine highlighted anew a problem which has been too long neglected, but which is growing rapidly in importance and cannot be stressed too strongly. The need for a thorough training of medical students in the principles and practical applications of medical genetics is becoming more apparent with each new discovery in the field.

At this gathering Dr. H. J. Muller, who received the Nobel Prize in Medicine for 1946, discussed the question of the accumulation of mutations in human populations, both from natural causes and from artificial radiation, including x-rays and the emanations from nuclear fission such as those used in the atomic bomb. He presented valuable suggestions for "mutational prophylaxis."

Dr. Laurence H. Snyder of the Ohio State University, in 1940, in the Biggs Lecture on Medical Genetics and Public Health, then discussed the training of physicians in this field. He pointed out that the adequate understanding of Dr. Muller's important presentation, which has a bearing on the lives of all of us, is dependent upon a knowledge of the basic principles of heredity. Furthermore, the physician needs not only a basic acquaintance with genetics, but a specialized knowledge of medical genetics, because of the very practical benefits which this knowledge may bring to the practice of medicine.

Dr. Madge T. Macklin has for years stressed at every opportunity the need for medical genetics in the medical curriculum. At first only a voice crying out in the wilderness, she has been joined by a veritable chorus.

Medical schools are slowly but surely responding to this challenge. Fifteen years ago Macklin conducted a survey which revealed the fact that not a single medical school at that time offered a course in medical genetics, and only two schools presented any material on the subject in other courses. Snyder has also presented the results of a similar survey just completed. Today three medical schools have required courses in medical genetics, four have elective courses, and ten more are planning to present such courses in the near future.

In addition, forty-two medical schools actively present material on medical genetics in connection with didactic or clinical courses.

This progress is highly commendable, but much remains to be done. Every premedical student should be required to take a course in the principles of genetics, and every medical student should have training in medical genetics and its practical applications. Only then will the remarkable strides in this medically important science be made functional and profitable. To those engaged in obstetric practice, these facts are of particular import.

American Journal of Obstetrics and Gynecology, George W. Kosmak, M.D., Editor, p. 351, August 1947.

ACQUIRED RESISTANCE TO ANTIBIOTICS

IT HAS long been recognized that microorganisms may acquire a degree of resistance to a drug as a result of exposure to sublethal concentrations, although originally they were highly sensitive to the drug's action.

Many highly susceptible species of organisms, such as the pneumococcus, the streptococcus and the gonococcus, have been found capable of acquiring such resistance to the sulfonamides. This is also true of the antibiotics penicillin and particularly streptomycin.

It is an interesting and practically important fact

that acquired resistance to either the sulfonamides, penicillin, or streptomycin does not affect the original susceptibility of the strain to the other drugs. The precise mechanism or site of their action is evidently different.

There are two obvious ways in which a strain of organisms might become resistant. Exposure to a sublethal concentration of the drug might bring about an adaptation as the result of a gradual progressive change in the metabolic activities of the bacterial population as a whole. This exposure, however, might operate by killing or inhibiting the growth of the sensitive individuals and permit a few initially resistant organisms to outgrow and replace the others. The former hypothesis seems inherently improbable because of the great rapidity with which a strain may become resistant, even within twenty-four hours in the case of one H. *influenzae* strain. Recent investigations to determine this point have furnished strong direct evidence in favor of the latter alternative.

Alexander and Leidy have reported careful studies of 14 strains of Type b *Hemophilus influenzae* derived from human infections, with respect to their sensitiveness to streptomycin. All the strains initially were sensitive to streptomycin. growth being inhibited by from 1 to 13 units per cc. of medium when ordinary inocula containing from 1 million to 1700 million organisms were used. Ten patients recovered under treatment, but four did not respond to streptomycin. In three of these cases, subsequent cultures yielded strains which were resistant to this drug, growing well in media containing 1000 units per cc.

They searched for individual organisms which were resistant to streptomycin in 10 of the initial (sensitive) strains by inoculating large quantities (142 billion to 522 billion organisms) on media containing 1000 units of streptomycin per cc. In every case a small number of colonies of resistant organisms appeared, the incidence varying from about 1:1 billion to 1:14 billion organisms. There was no correlation between the relative number of resistant organisms found in the original cultures and the subsequent development of drug-resistance during treatment.

The relative number of colonies of resistant organisms seemed to depend principally upon the size of the original bacterial population cultured. Patients with severe infections and relatively large numbers of organisms in their tissues would therefore be much more likely than those with milder infections to harbor a sufficient number of drug-resistant organisms to overgrow the others and produce a resistant strain.

Miller and Bonnhoff have reported similar studies of 18 strains of meningococci which were sensitive to streptomycin.

The source of the few initially resistant organisms in these cultures is a matter of interest. Alexander and Leidy have advanced evidence to show that they possess the characteristics of bacterial mutants. Thus, there is a marked variation in the number of resistant individuals in different cultures of the same strain, depending upon how early in the growth of the culture the first resistant mutants happened to appear.

The calculated rate of occurrence of resistant individuals is very low, about 1/20 billion per bacterium per bacterial generation, and it was relatively constant for the different strains. The trait was transmitted unchanged through many generations. Miller and Bonnhoff concur in regarding their variants as mutations.

Accepting the hypothesis that the resistant organisms are mutants, this observation may be in part explained by the fact that in well treated patients the multiplication of the sensitive organisms is promptly stopped and there is a smaller bacterial population from which resistant mutants might arise. There is reason to believe that the outcome depends in part upon the number of such resistant organisms present.

Another point of practical significance is the fact that organisms which become resistant to one antibiotic retain their original sensitiveness to others. This makes it rational to administer them in combination when it is feasible to do so. The few variants of H. *influenzae* which are resistant to streptomycin, e.g., retain their sensitiveness to sulfonamides, and there is a better chance of eliminating the infection completely if both drugs are administered.

Annals of Internal Medicine, Vol. 27, p. 317, August 1947.

New Drugs

Information published in this department has been supplied by the manufacturers of the products described

PROPYL THIOURACIL TABLETS LEDERLE

PURPOSE AND INDICATIONS: For the treatment of thyrotoxicosis (Graves disease) both for preoperative preparation of patients with hyperthyroidism for thyroidectomy, and for medical treatment alone.

COMPOSITION: Propyl Thiouracil Tablets Lederle contain 50 mg. of 6-n-propyl thiouracil per tablet.

DOSAGE: Initial daily dose of 75 to 300 mg. divided into three doses at eight-hour intervals. Severe and moderately severe cases in adults usually require daily doses of 150 mg. to 300 mg. initially. Less severe cases may respond to as little as 75 mg. daily. When the patient has responded to treatment the daily doses may be reduced to 50 mg. according to the individual response.

CAUTIONS: Few toxic side effects have been reported, but, like thiouracil, propyl thiouracil is a potent drug with potentialities for the same type of reactions. White blood cell counts, including differentials, and constant observation of patients are always essential. Dermatitis, drug fever, leukopenia, some degree of granulocytopenia, and gastrointestinal upsets have been reported in a few cases.

HOW SUPPLIED: In bottles of 100 and 1,000 tablets.

PRICE: 100 tablets $2.65 list; 1,000 tablets $22.50 list.

PRODUCER: Lederle Laboratories Division American Cyanamid Company, Pearl River, New York.

PENICILLIN CALCIUM BUFFERED TABLETS—CUTTER

PURPOSE: Oral treatment of low grade infection.

DESCRIPTION: Each tablet contains 10,000 units of calcium penicillin buffered with 0.4 gm. of calcium carbonate. They may be stored at room temperature for twelve months without any significant loss of potency.

INDICATIONS FOR USE: They may be used prophylactically in rheumatic or congenital heart disease when tonsillectomy or tooth extraction is planned. In pneumococcic, streptococcic and staphylococcic infections, they are effective used following the acute phase, during which penicillin has been administered parenterally.

HOW SUPPLIED: Screw-top bottles of 12 tablets.

PRODUCER: Cutter Laboratories, Berkeley 1, Calif.

CYTORA "ROCHE-ORGANON"

PURPOSE: A modern hematinic for hypochromic anemias.

COMPOSITION: Each Cytora tablet contains: Folic acid, 0.75 mg; exsiccated ferrous sulfate, 100 mg; liver concentrate (1.20), 150 mg; vitamin C, 25 mg; vitamin B_1, 1 mg; vitamin B_2, 1 mg; vitamin B_6, 0.5 mg; niacinamide, 5 mg; calcium pantothenate, 1 mg; plus other factors naturally present in liver concentrate.

DESCRIPTION: Cytora supplies iron, folic acid, and other dietary factors utilized for erythropoiesis.

INDICATIONS FOR USE: Recommended for hypochromic anemias: Anemia of blood losses (surgery, peptic ulcers, bleeding hemorrhoids, carcinoma of the stomach or bowel, ulcerative colitis, tuberculosis, hookworm infestation, amebic dysentery and purpura), nutritional anemia, anemia of pregnancy and lactation, anemia in the aged, anemia of hypermenorrhea, anemia of childhood, postinfectious anemia, convalescence and general debility.

DOSAGE: Recommended dose two tablets three times a day with or immediately after meals; for maintenance therapy after the blood has been restored to normal, two tablets per day.

HOW SUPPLIED: In bottles of 100, 250, and 1,000 tablets.

PRODUCER: Roche-Organon, Inc., Nutley 10, N. J.

TRI-SULFANYL

PURPOSE: For treatment in all conditions amenable to sulfathiazole, sulfadiazine, or sulfamerazine.

COMPOSITION: Three sulfonamides combined. Each teaspoonful syrup (5 cc.) or one tablet contains 7½ gr. of sulfa compound; sulfathiazole 0.162 gm. (2.5 gr.), sulfadiazine 0.162 gm., sulfamerazine 0.162 gm., all *microcrystalline*. In syrup only—sodium citrate 5.79 gr. in a pectinized, vanilla flavored sugar base. This combination reduces danger of renal damage to a minimum.

DOSAGE: Eight tablets or teaspoonfuls of syrup, then 2 tablets or teaspoonfuls of syrup every four hours.

HOW SUPPLIED: Syrup—4 oz., 8 oz., 16 oz.
Tablets—50, 100, 250, 500, 1000.

PRODUCER: Casimir Fund Laboratories, Inc. (affiliate of U. S. Vitamin Corporation), 250 East 43rd Street, New York 17, N. Y.

FURACIN SOLUTION IN A LIQUID VEHICLE

PURPOSE: An antibacterial agent for use where the ointment form is inconvenient or contraindicated—chiefly on wet dressings.

COMPOSITION: Furacin Solution contains:

	Per Cent
Furacin (brand of nitrofurazone: 5-nitro-2-furaldehyde semicarbazone)	0.2
Polyethylene glycol of mon-iso-octyl phenyl ether (wetting agent)	0.3
Carbowax (brand of polyethylene)	65.0
Water	34.5

DESCRIPTION: Yellow liquid with a viscosity twice that of water, and slightly hypertonic; stable under all usual climatic conditions. Because Furacin is discolored by light, it is dispensed in amber bottles and should not be left in sunlight. It should not be placed in metal containers. Furacin Solution has the same wide antibacterial spectrum as has Furacin Soluble Dressing, affecting many gram-positive and gram-negative bacteria found in surface infections.

INDICATIONS FOR USE: Same as for Furacin Soluble Dressing; for infected surface wounds, or for the prevention of such infection; infections of second and third degree burns; carbuncles and abscesses after surgical intervention; infected varicose ulcers; infected superficial ulcers of diabetics; impetigo of infants and adults; treatment of skin-graft sites; osteomyelitis associated with compound fractures in conjunction with indicated surgical intervention; secondary infections following dermatophytoses.

CAUTION: Although no cases of sensitization to Furacin Solution have as yet occurred in preliminary studies, it is to be expected that such will occur, as with Furacin Soluble Dressing—in approximately 4 per cent of cases. Furacin is a powerful antibacterial agent; it is *not* a "healing agent." As soon as Furacin has cleared an infection, it is advisable to use some bland preparation until healing is complete. Long continued, daily applications of Furacin may increase susceptibility to sensitization.

HOW SUPPLIED: Now available to pharmacies and hospitals for prescriptions, in 4 oz. and one pint bottles, at $1.75 and $4.75 respectively.

PRODUCER: Eaton Laboratories, Inc., Norwich, N. Y.

STREPTOMYCIN MERCK

PURPOSE: Streptomycin is an antibacterial agent of low toxicity, possessing selective therapeutic activity against a variety of pathogenic organisms.

DESCRIPTION: Streptomycin in dry form may be stored at room temperature, not exceeding 30° C. (86° F.), for periods up to one year without significant loss of potency. It should be stored in its original unopened container to prevent contamination and deliquescence.

INDICATIONS FOR USE: For treatment of infections due to susceptible gram-negative organisms.

DOSAGE AND METHOD OF ADMINISTRATION: At present, the three most common methods of administering streptomycin are subcutaneously, intramuscularly, and intrathecally. Dosage requirements vary with the sensitivity of the pathogen to the drug, the severity and location of the infection, and the presence of bacteremia.

CAUTIONS: Streptomycin is not to be regarded as a substitute for adequate surgical drainage or for the use of other therapeutic agents whose value in a given disease has been established.

HOW SUPPLIED: As the hydrochloride in rubber-stoppered, aluminum-capped vials. Since the total weight of the powder in the vial exceeds the amount of streptomycin base stated on the label it is recommended that the entire content of the vial be dissolved in a known volume of a suitable solvent, such as sterile, pyrogen-free distilled water or physiologic saline solution, and that an aliquot of this solution containing the desired dose be used for administration or for the preparation of more dilute solutions. Only clear solutions, free from undissolved particles, should be used parenterally or intrathecally.

PRODUCER: Merck & Co., Inc., Rahway, N. J.

LIQUOID MER-DIAZINE

PURPOSE: Chemotherapeutic agent against infections; prophylactic in wound infections, compound fractures, burns, etc., to supplement local therapy.

COMPOSITION: A palatable homogenized suspension containing per fluid ounce:

Sulfamerazine 1.5 gm. Sulfadiazine 1.5 gm.

INDICATIONS FOR USE: Infections caused by hemolytic streptococcus, pneumococcus, staphylococcus, meningococcus, gonococcus, Friedlander's bacillus, gas bacillus, aerobacter aerogenes, and other non-specific organisms causing urinary tract infections.

DOSAGE AND METHOD OF ADMINISTRATION: Children (up to 120 lbs. in weight)—30 mg. total sulfonamides per pound of body weight in 24 hours, divided into 6 equal doses. Adults—Initial 3-4 gm. dose, followed by 1 gm. every 6-8 hours thereafter, until temperature has remained normal for 48 to 72 hours. In very severe infections, the dosage may be increased 50 per cent.

CAUTIONS: Constant observation for toxic reactions is essential.

HOW SUPPLIED: Bottles of 4 fluid ounces and one pint.

PRODUCER: McNeil Laboratories, Inc., Philadelphia 32, Pa.

After Hours

POSTGRADUATE ACTIVITIES BEFORE AND AFTER KELLOGG

The conference of Graduate and Postgraduate Medical Education held in the Rackham Building, University of Michigan, early in the summer, was a great success.

Deans of medical schools and directors of the services at the Universities of New York, Duke, Minnesota, Columbia, Emory, George Washington, Colorado, Iowa, Michigan, Meharry, Washington, Cornell, Oregon, Illinois, Tufts, and Virginia were called together by *Benjamin Horning* of the W. K. Kellogg Foundation. These institutions were recipients of grants from the Foundation for the purpose of developing or strengthening their graduate and their postgraduate programs.

Moderators of the sessions were *Harold S. Diehl* (Minnesota), *A. C. Furstenberg* (Michigan), *Joseph C. Hinsey* (Cornell), *Currier McEwen* (New York University), *Howard H. Cummings* (Michigan), and *Samuel Proger* (Tufts). Each school reviewed its graduate and postgraduate activities before and after Kellogg.

Special discussion subjects were: (1) The Graduate Training and Continued Education of the General Practitioner, (2) The Teaching of the Basic Sciences at the Graduate Level, and (3) Regionalization of Medical Education.

The directors of the services learned that they had a great deal in common when they started discussing the merits and demerits of their programs, while the deans and others discussed the subject from the administrators' standpoint.

On the second evening we were royally entertained by the Michigan group. Following this there was a dinner at which *Salvador Zubiran,* Rector of the National University of Mexico, spoke. He gave us an insight into Mexican University life and his proposed expansion program. Unique indeed was the manner of arranging the buildings, and their purposes. There was to be a covered walk for students and a large stadium for athletics.

We also saw the Navy film on the Bikini party which was noisy and colorful. The possibilities of atomic warfare were explained by *Dean Sawyer* of the graduate school.

A splendid gesture was extended by the W. K. Kellogg Foundation in inviting *Lester J. Evans* of the Commonwealth Fund to take part in the discussion. There was a great deal of debate on the basic sciences. . . . *C. E. de la Chapelle* gave a dynamic description of New York University's fine plan. . . . *Wilburt C. Davison* who sounds like Orson Welles and looks like a character in a detective story (minus the peaked fore and aft hat), explained Duke's plans. Well known author of the *Compleat Pediatrician,* he is a stimulating person. He told me he wrote the book from the notes which he compiled as a student and later as a physician. He published his own book when he learned what the terms of the book publishers were to be.

He has a standing offer of a dime for every error found by students. As a result it has fewer errors than many textbooks. A student who wishes to take his girl to the movies reads the book until he has found the proper number of errors and then collects.

Columbia's Assistant Dean, *John B. Truslow,* gave a scholarly report of their program. . . . *Hugh Wood* of Emory won many to his side when he doubted that a recent graduate who has only had three years of training in internal medicine could act as a consultant. He also felt that the men who are now receiving advanced training in internal medicine were going to make the best type of general family physician in the future.

Scholarly, quiet, dignified *Walter A. Bloedorn* told of the extensive program George Washington is developing. . . . *Ward Darley* is leading Colorado into new areas of expansion by cooperating with all existing agencies in the state. He came out of practice to take over the deanship and is doing a spectacular job.

C. F. Wilkinson, Jr., with his Atlanta accent, told of Michigan's plan of cooperating with smaller hospitals throughout the state in establishing training programs for residents. . . . *Murray C. Brown* gave us a real background picture of the Negro and his problems and pleaded for support for his group. . . . Handsome, energetic *Thomas M. Peery* is the sparkplug in the George Washington program. . . . Careful, meticulous *John E. Detrick* is doing a finished job at Cornell. . . . *Charles M. Holman,* a most promising young man, told of Oregon's fine program.